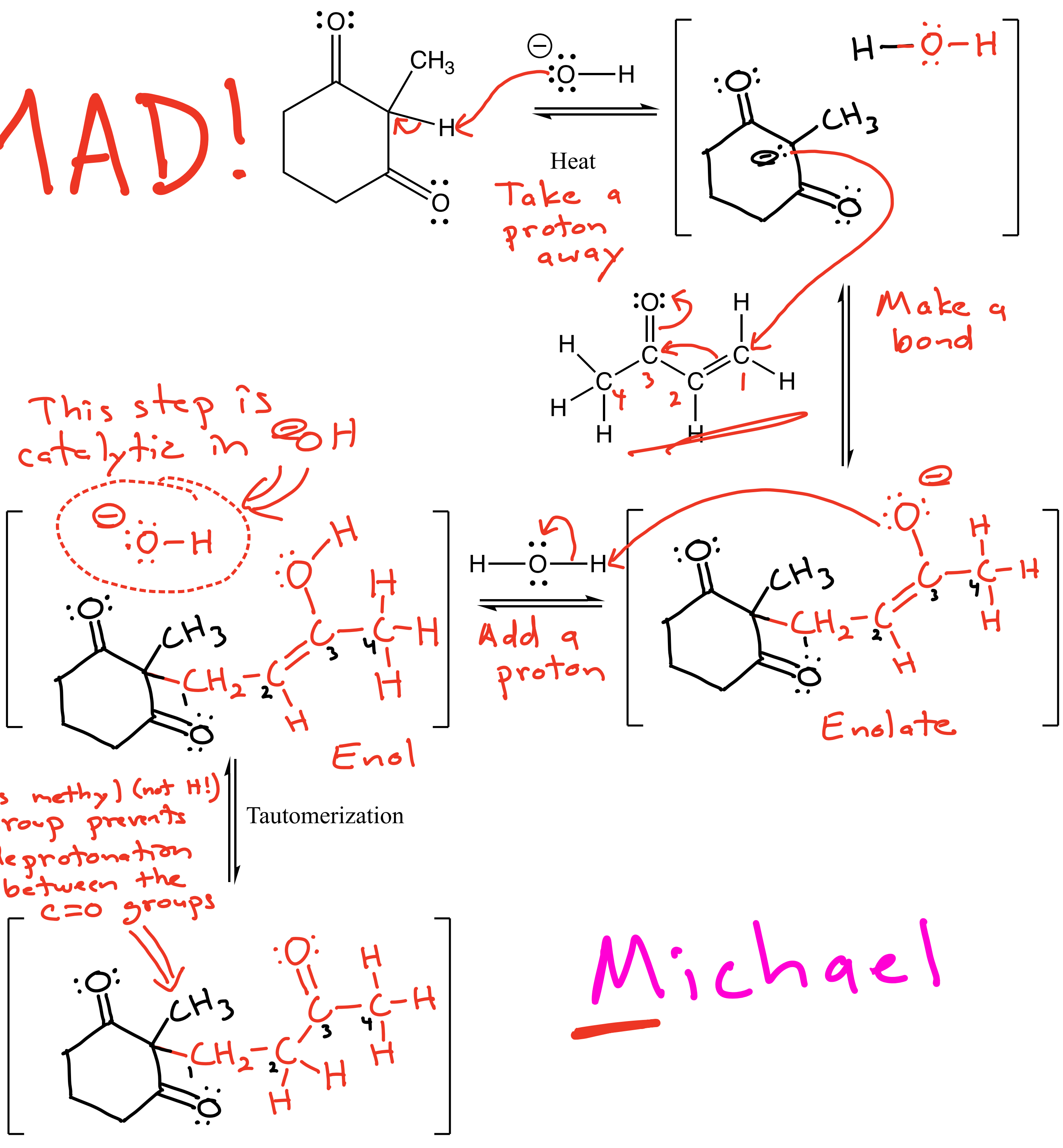
Is a Michael reaction followed by a Aldol reaction followed by dehydration

Robinson Annulation Part 1 - Michael Reaction Steps

MAD!



Take a proton away

Make a bond

Add a proton

Enolate

This step is catalytic in ⊖OH

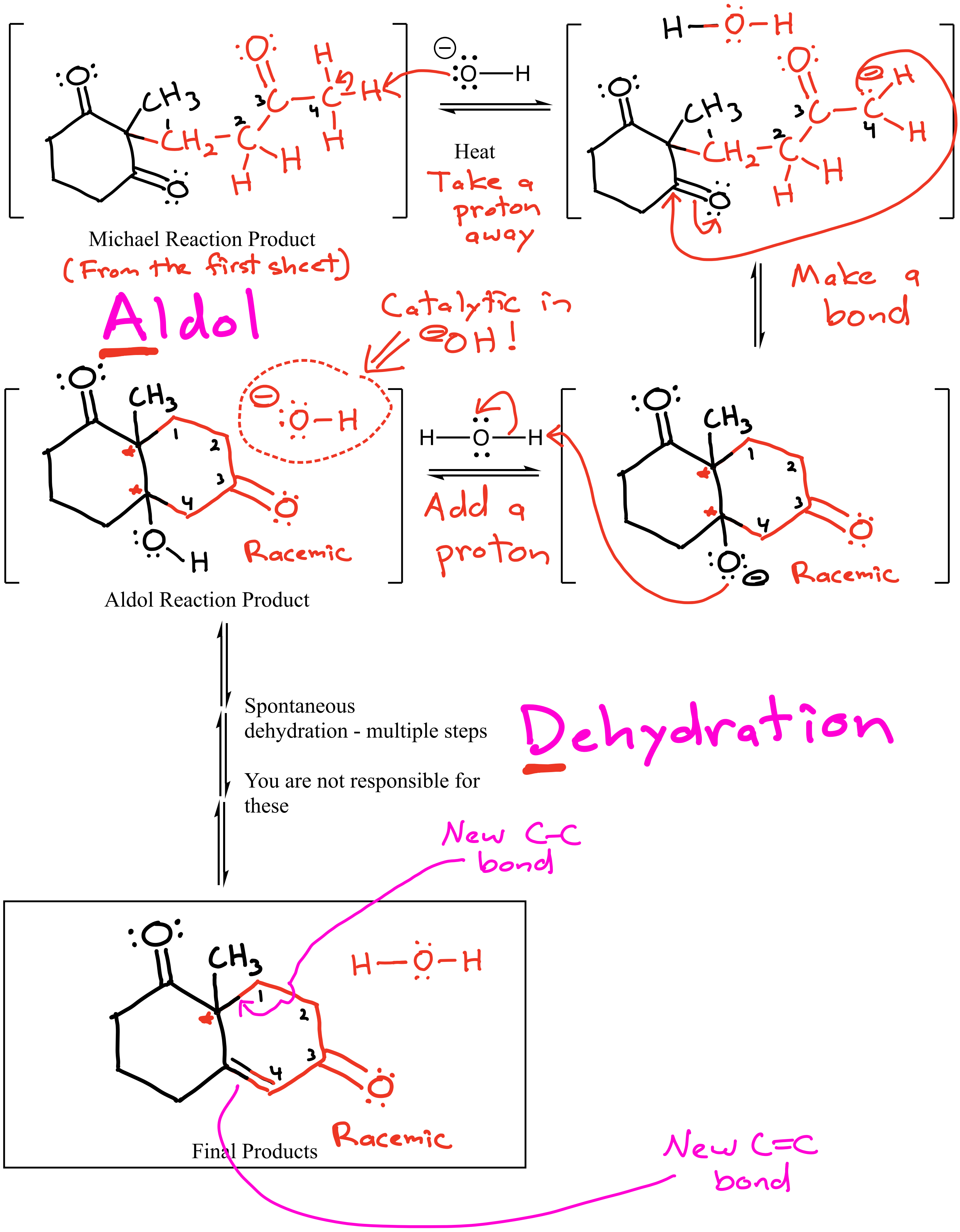
Enol

This methyl (not H!) group prevents deprotonation between the C=O groups

Michael Reaction Product

Michael

Robinson Annulation Part 2 - Aldol and Dehydration Steps



Michael Reaction Product

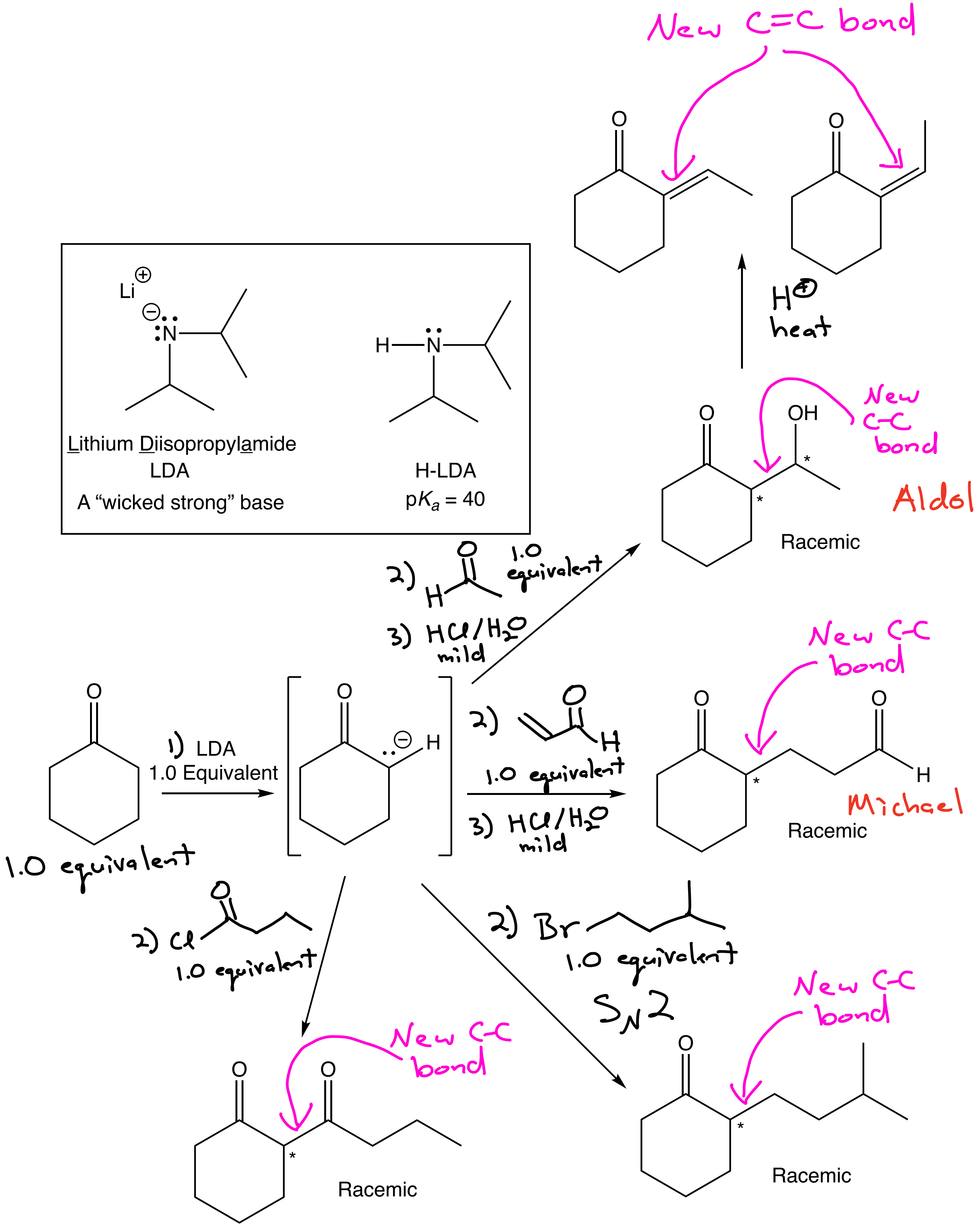
Heat

Aldol Reaction Product

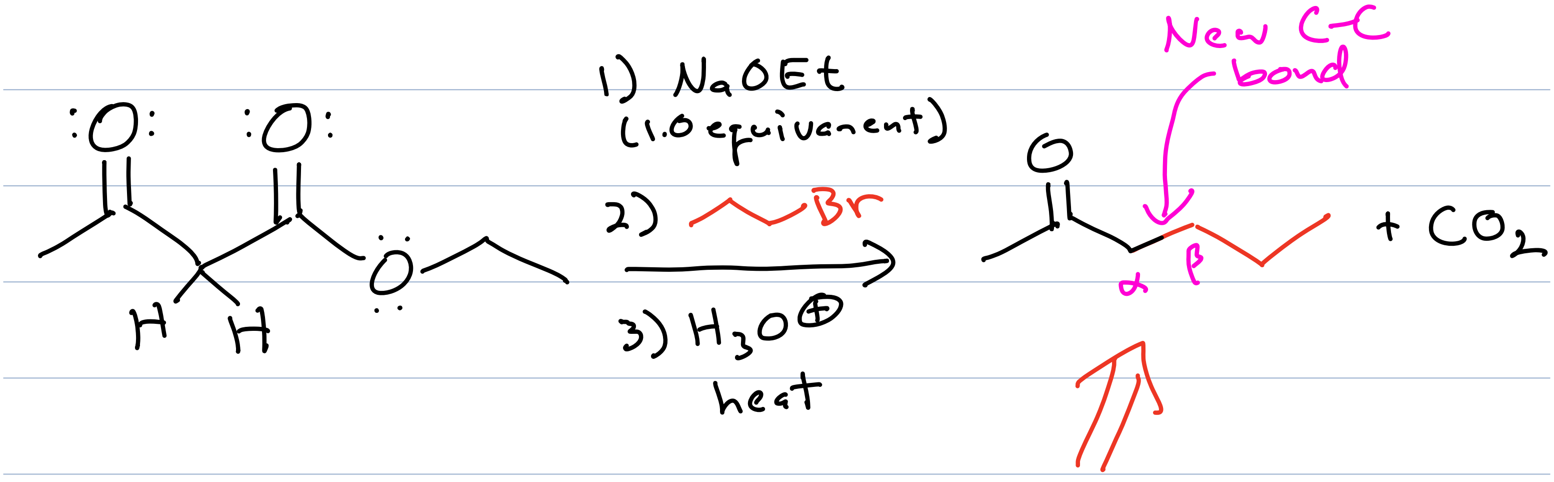
Spontaneous dehydration - multiple steps

You are not responsible for these

Final Products

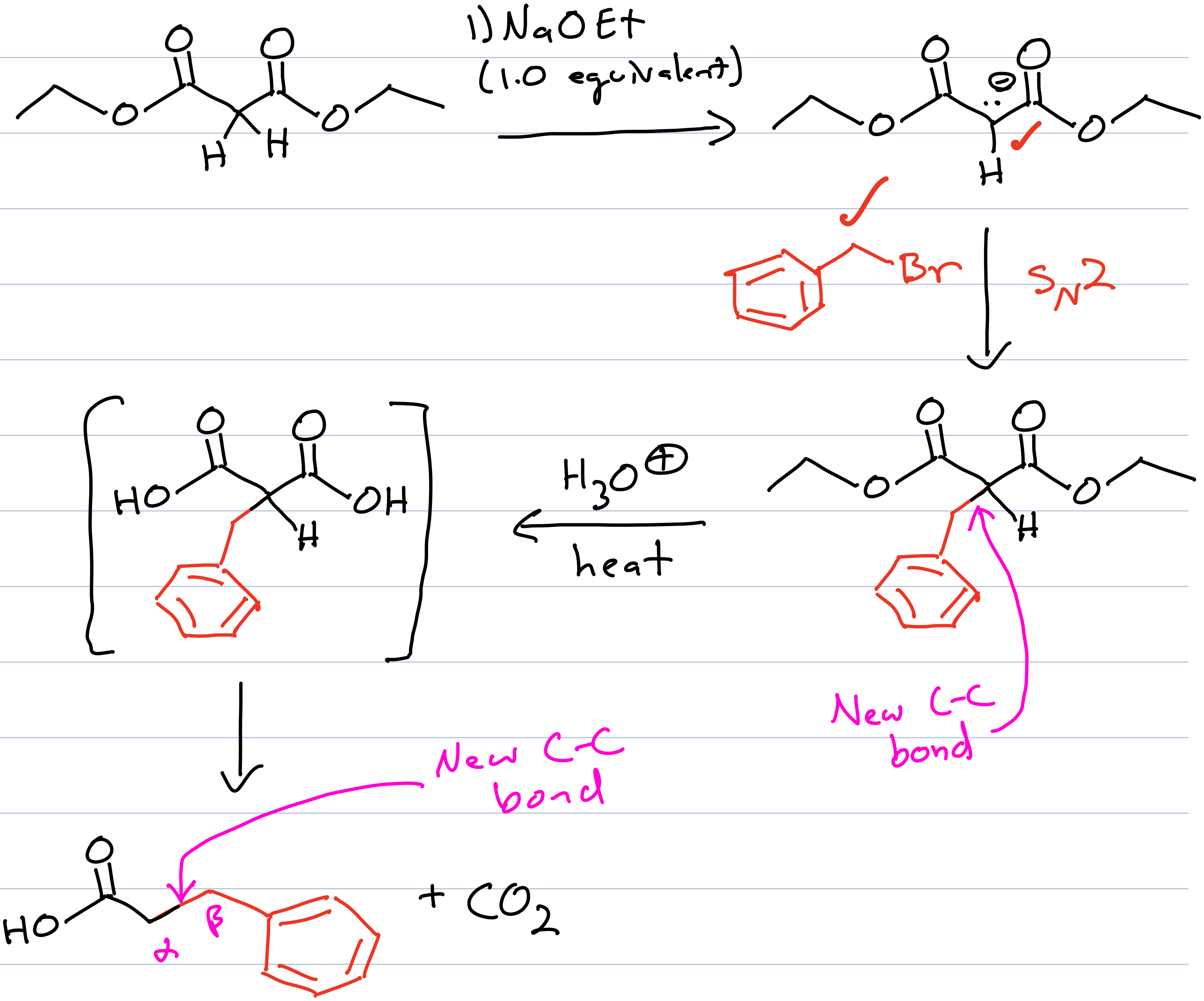

Li⊕
⊖:N̈
Lithium Diisopropylamide
LDA
A "wicked strong" base
H—N̈
H-LDA
pK_a = 40
O
1.0 equivalent
1) LDA
1.0 Equivalent
O
⊖ H
2) H(C=O)CH3 1.0 equivalent
3) HCl/H2O mild
O
OH
*
*
New C-C bond
Aldol
Racemic
H⊕
heat
O
O
New C=C bond
2) CH2=CHCHO 1.0 equivalent
3) HCl/H2O mild
O
O
H
*
New C-C bond
Michael
Racemic
2) Cl(C=O)CH2CH2CH3
1.0 equivalent
O
O
*
New C-C bond
Racemic
2) Br
1.0 equivalent
SN2
O
*
New C-C bond
Racemic

Acetoester Synthesis Summary



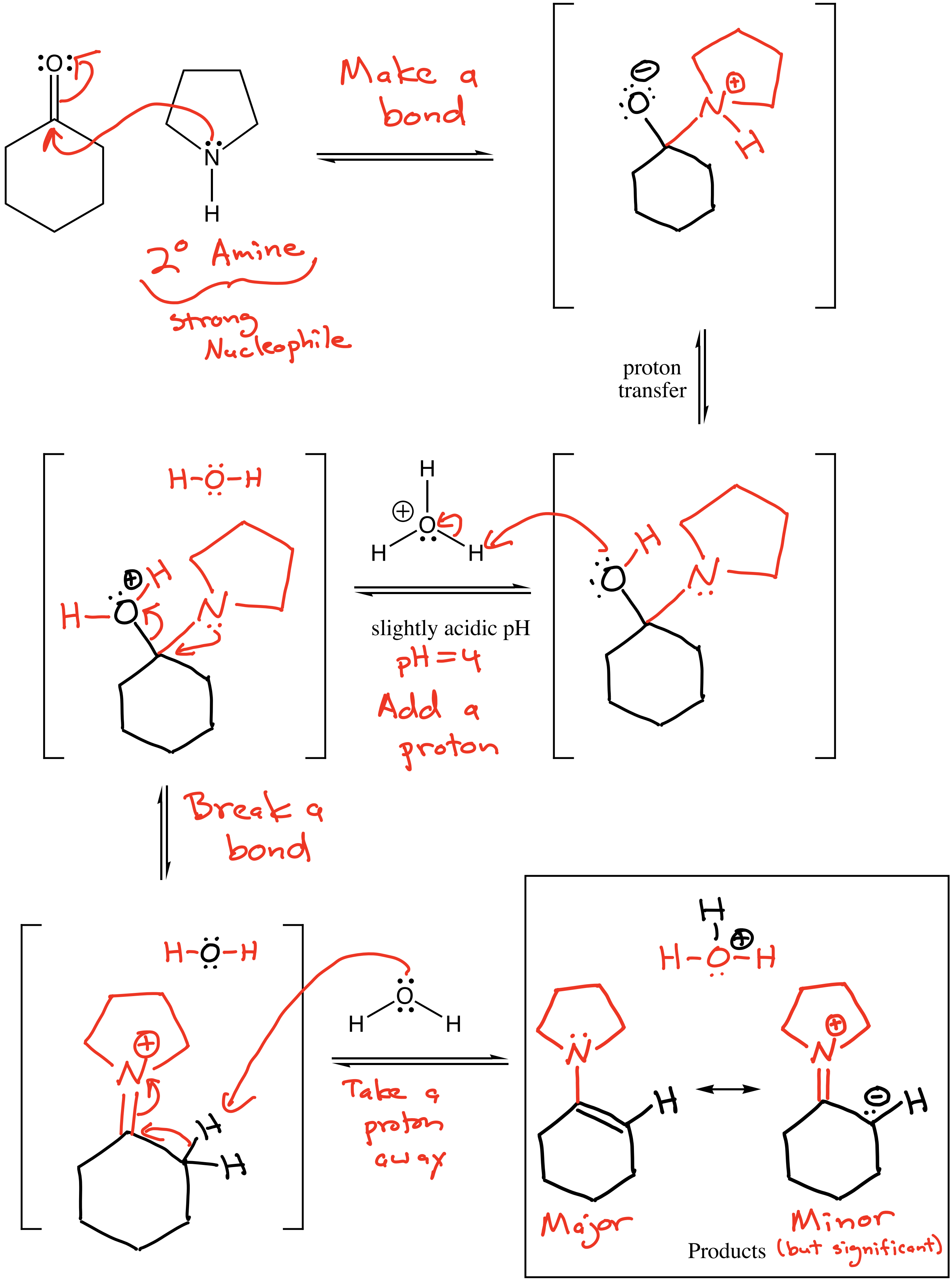
KRE – A methyl ketone with a new C–C bond between the α and β carbon atoms

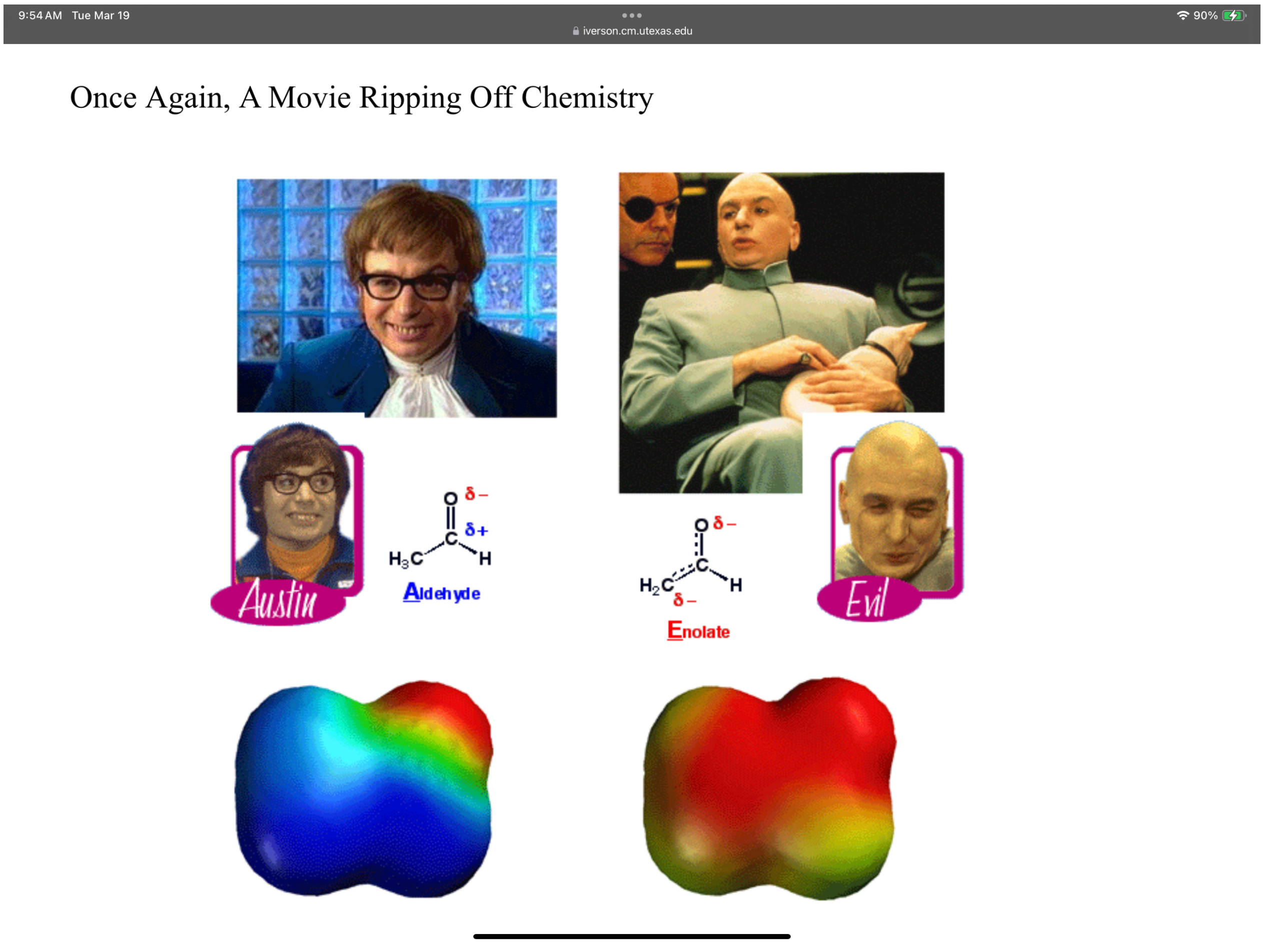
We start with diethyl malonate



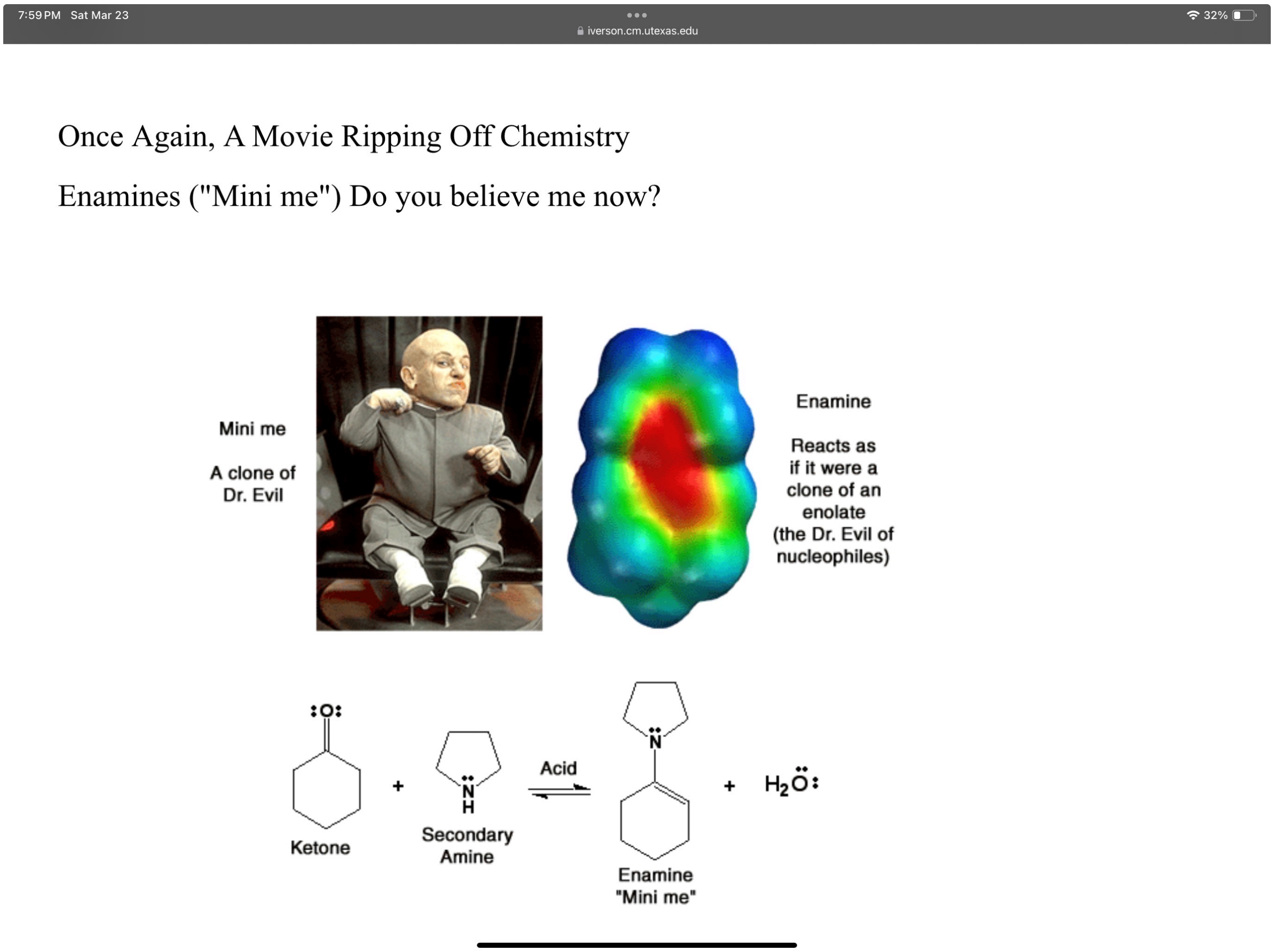
KRE → A carboxylic acid with a new C-C bond between the α and β carbon atoms

Enamine Formation





Once Again, A Movie Ripping Off Chemistry



Once Again, A Movie Ripping Off Chemistry

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

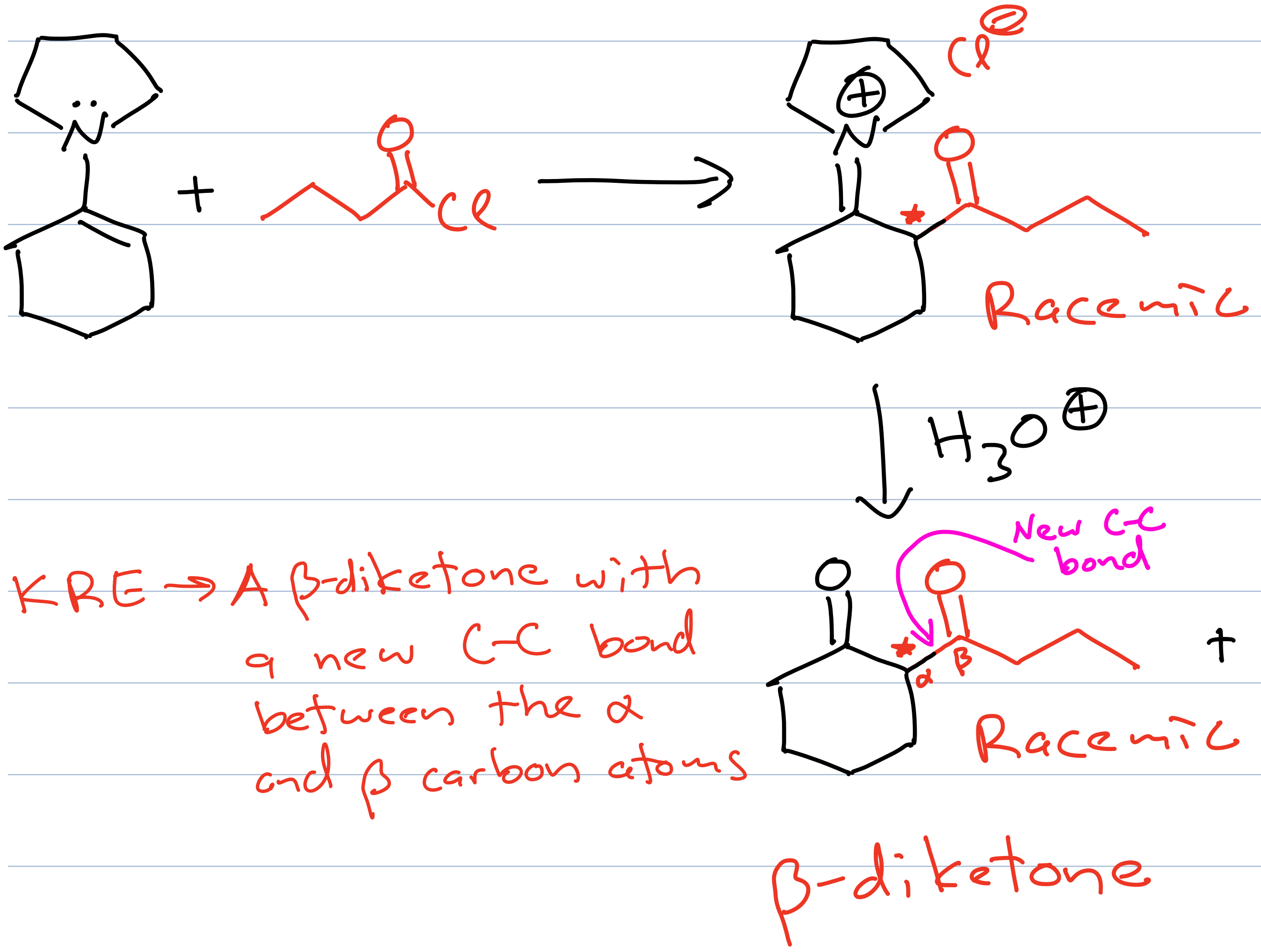
Mini me

A clone of Dr. Evil

Enamine

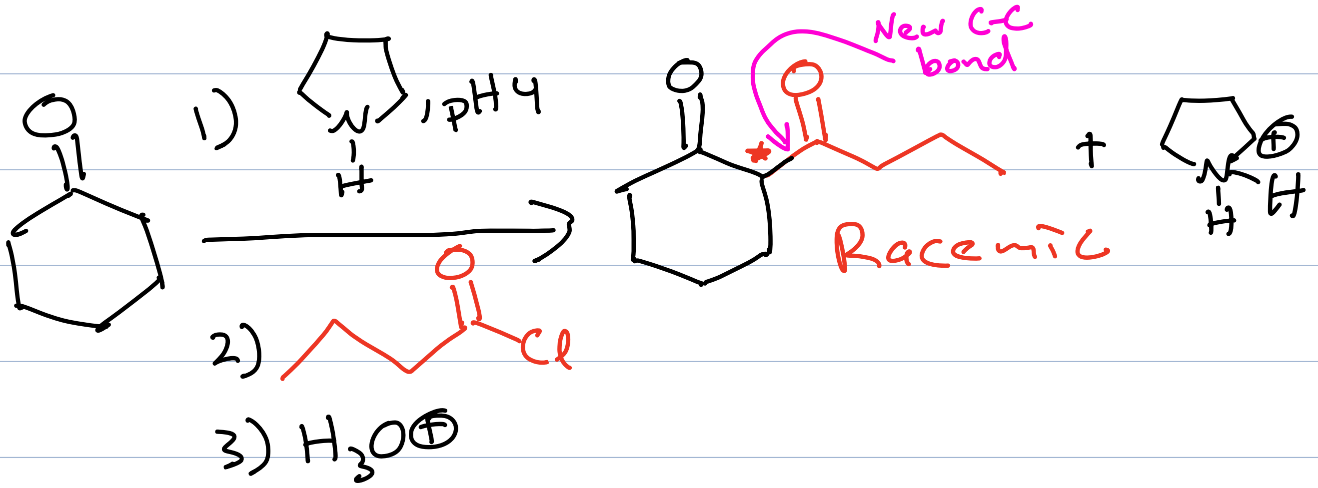
Reacts as if it were a clone of an enolate (the Dr. Evil of nucleophiles)

2) Acid chlorides ⇒ β-diketones



KRE → A β-diketone with a new C–C bond between the α and β carbon atoms

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

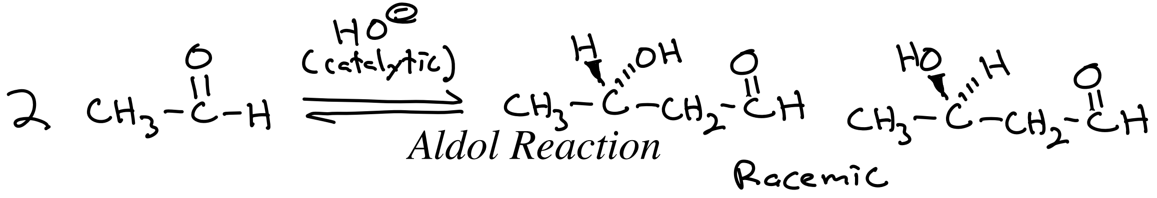
β-Diketone

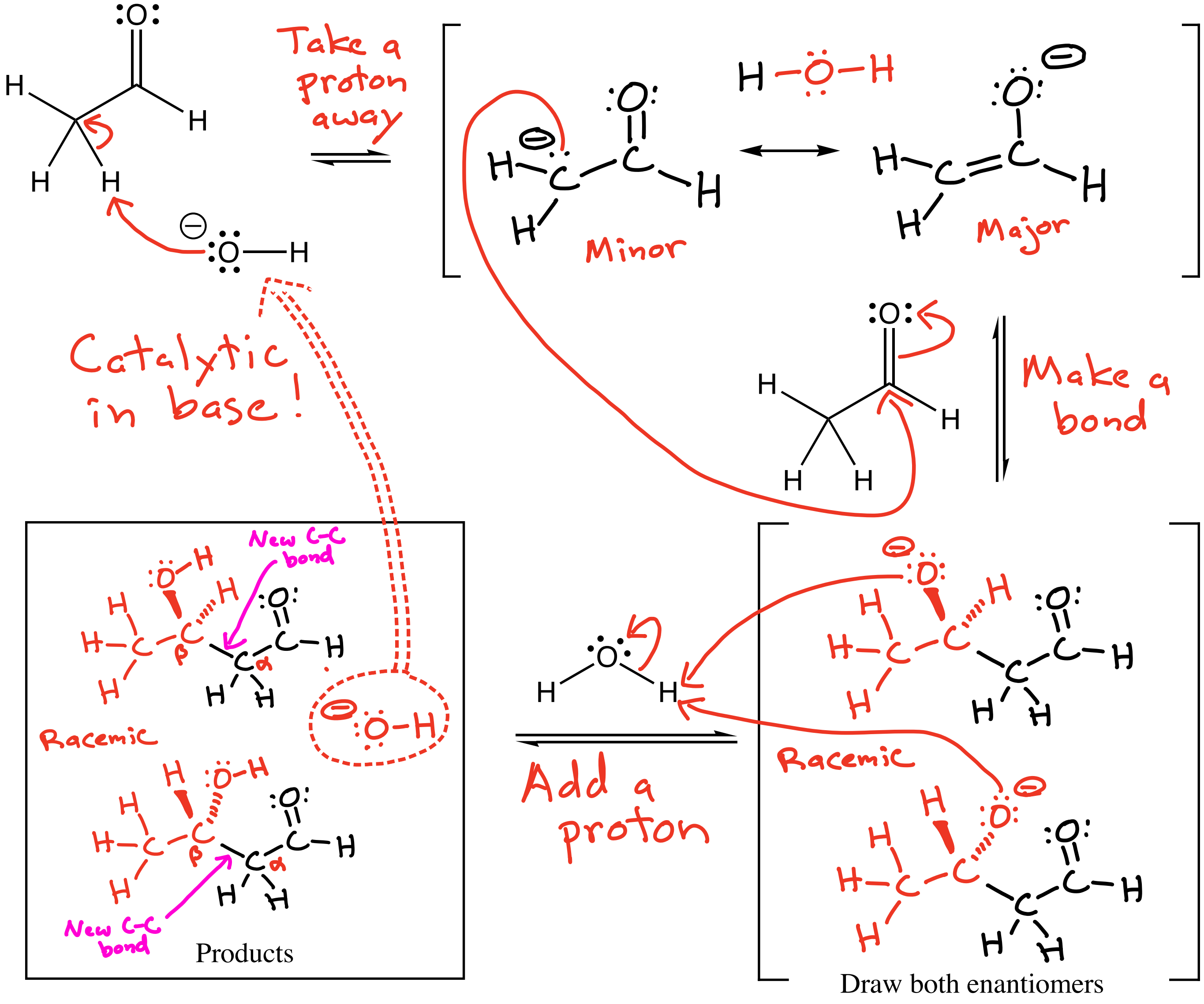
Carboxylic acids

Substituted aldehyde

Substituted ketone

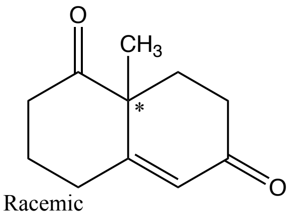
β-Diester



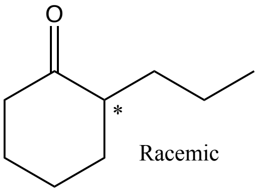


KRE → β-hydroxy aldehyde
with a new C–C
bond between the
aldehyde α and β
carbons

Mechanism
A



Racemic



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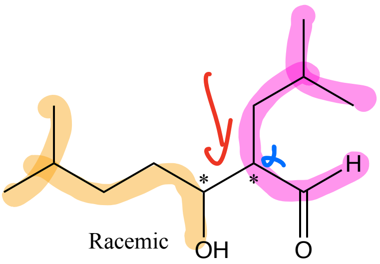

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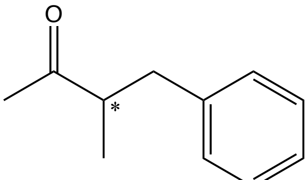

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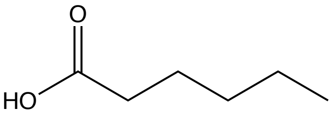

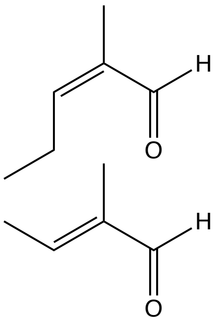

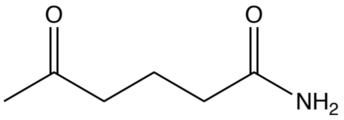

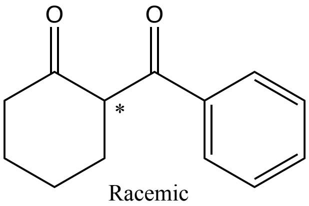

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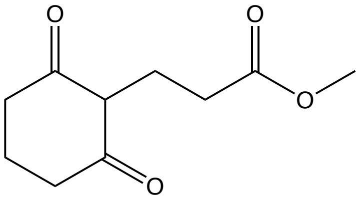

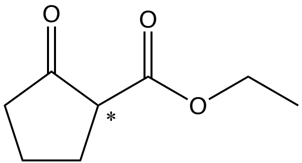

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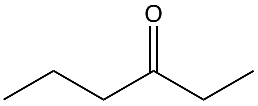

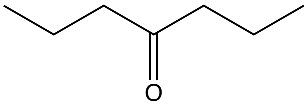

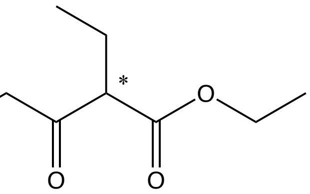

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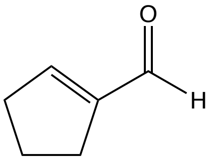
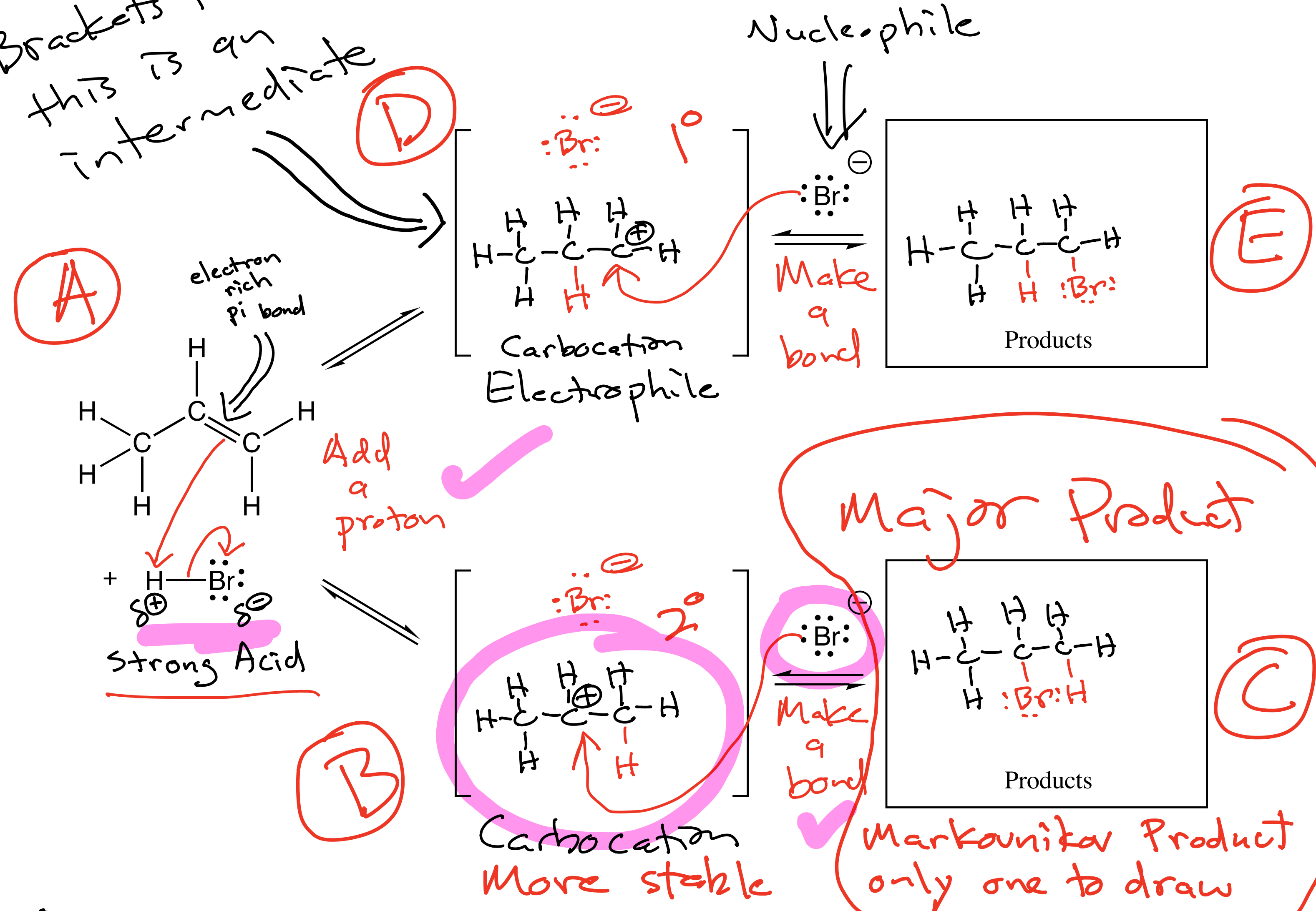



WAYNE'S WORLD

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

Addition of H-X to an Alkene

Brackets indicate this is an intermediate



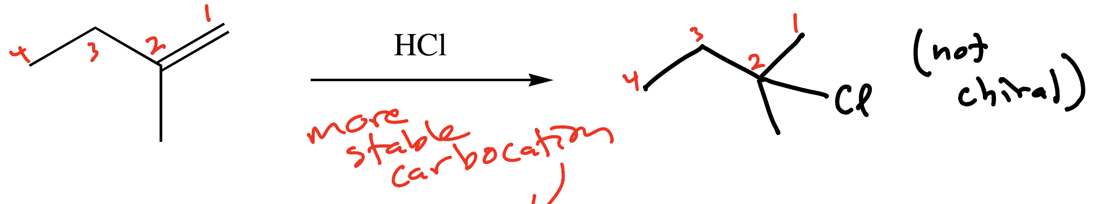
Which constitutional isomer is formed?

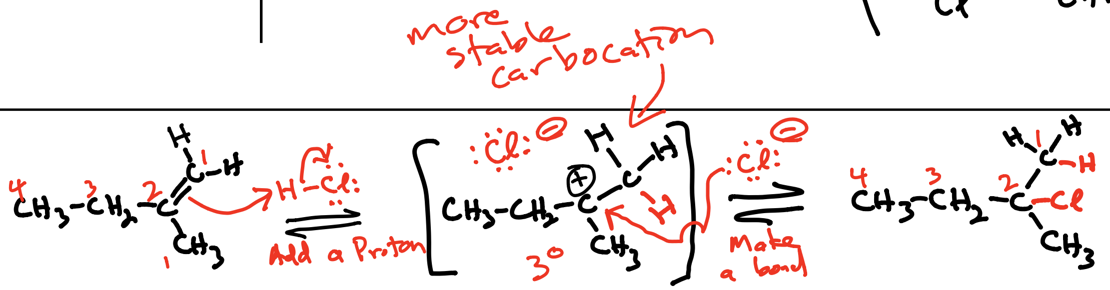
Summary: Alkene pi bond reacts with H-X to add a proton to create a carbocation intermediate that makes a bond with X⊖ to give the product

Regiochemistry: Markovnikov's Rule

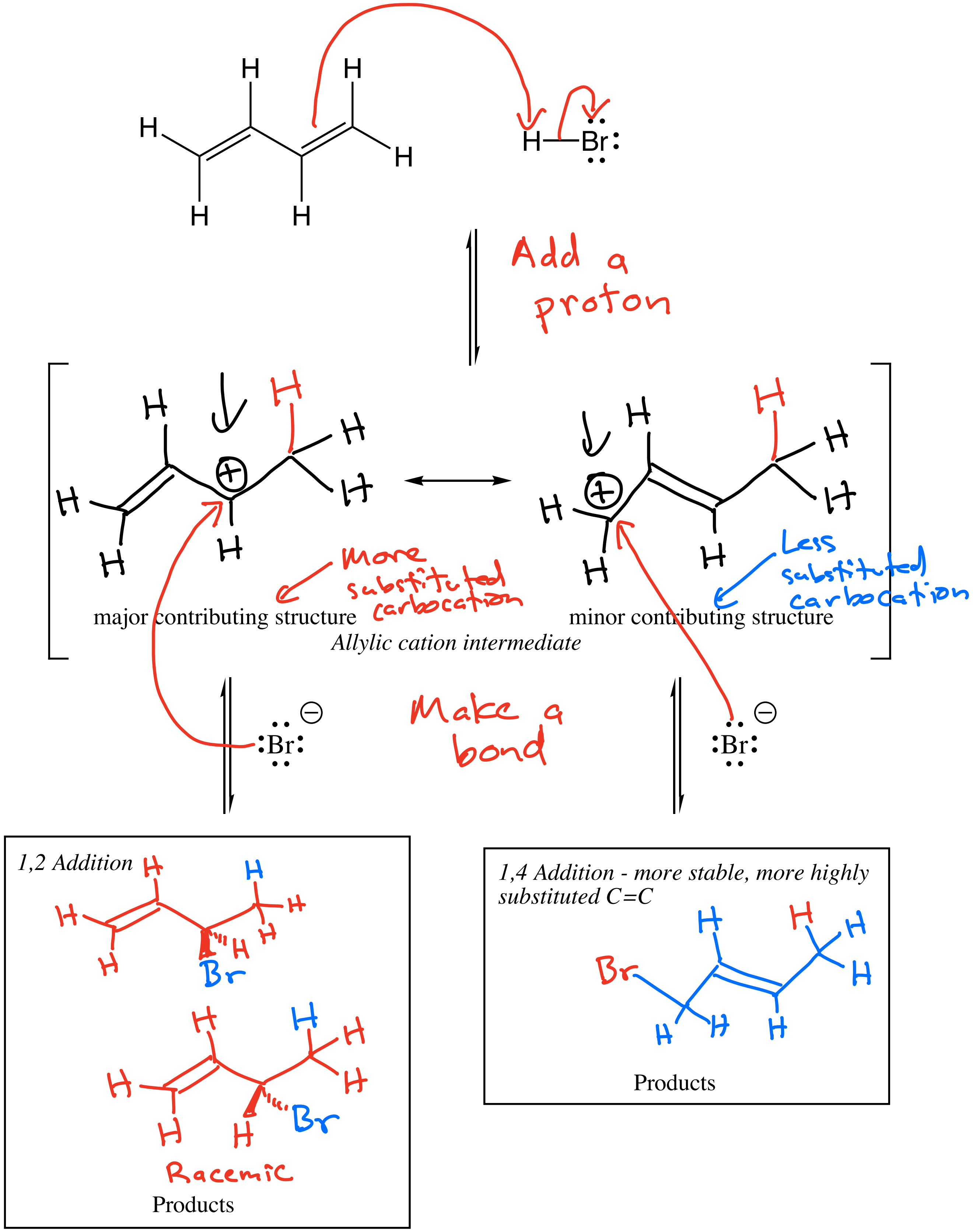
Stereochemistry: Mixed (time capsule) → Racemic Product

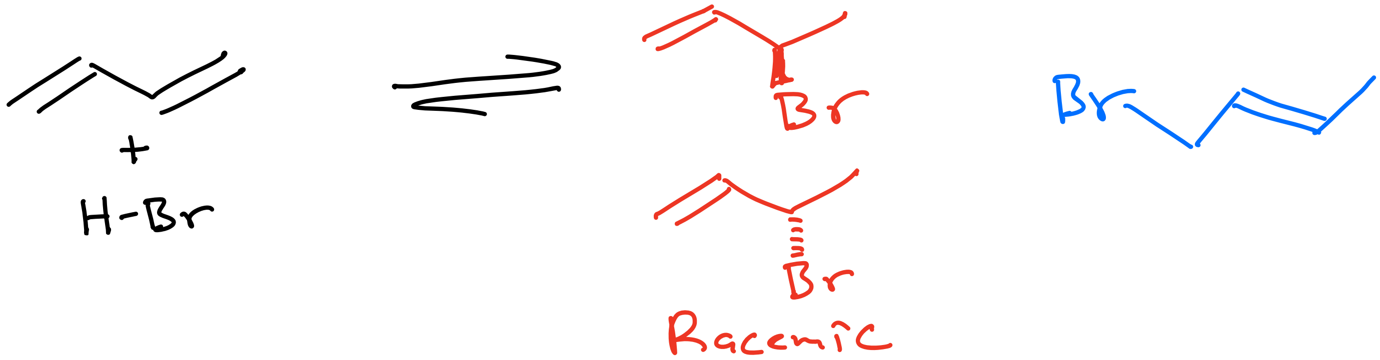
Example:



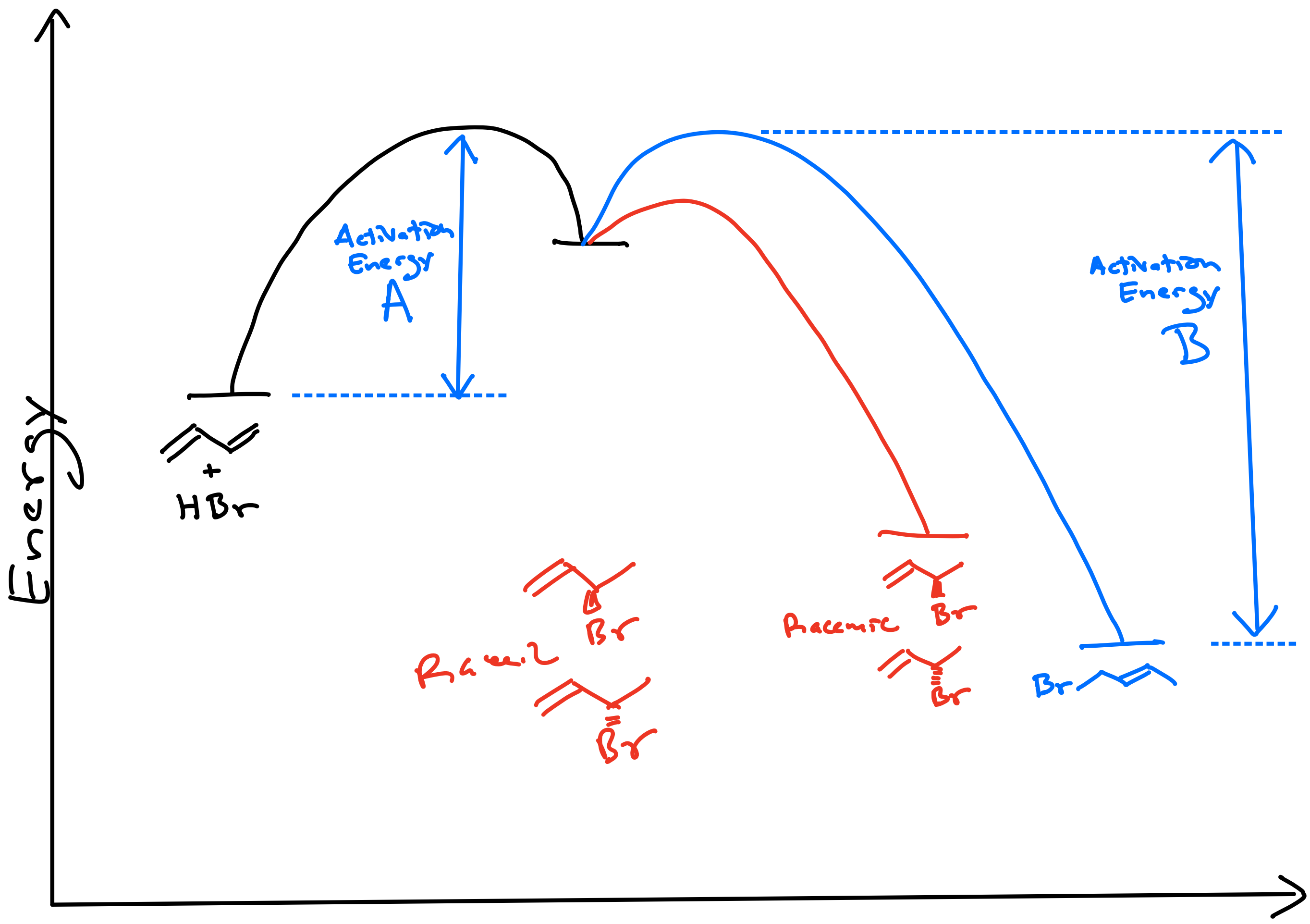


H-X reacting with conjugated dienes





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 and activation energy B

Thermodynamic Control

Most stable product wins

Electrons should be thought of as waves.

Orbitals are described by wave equations.

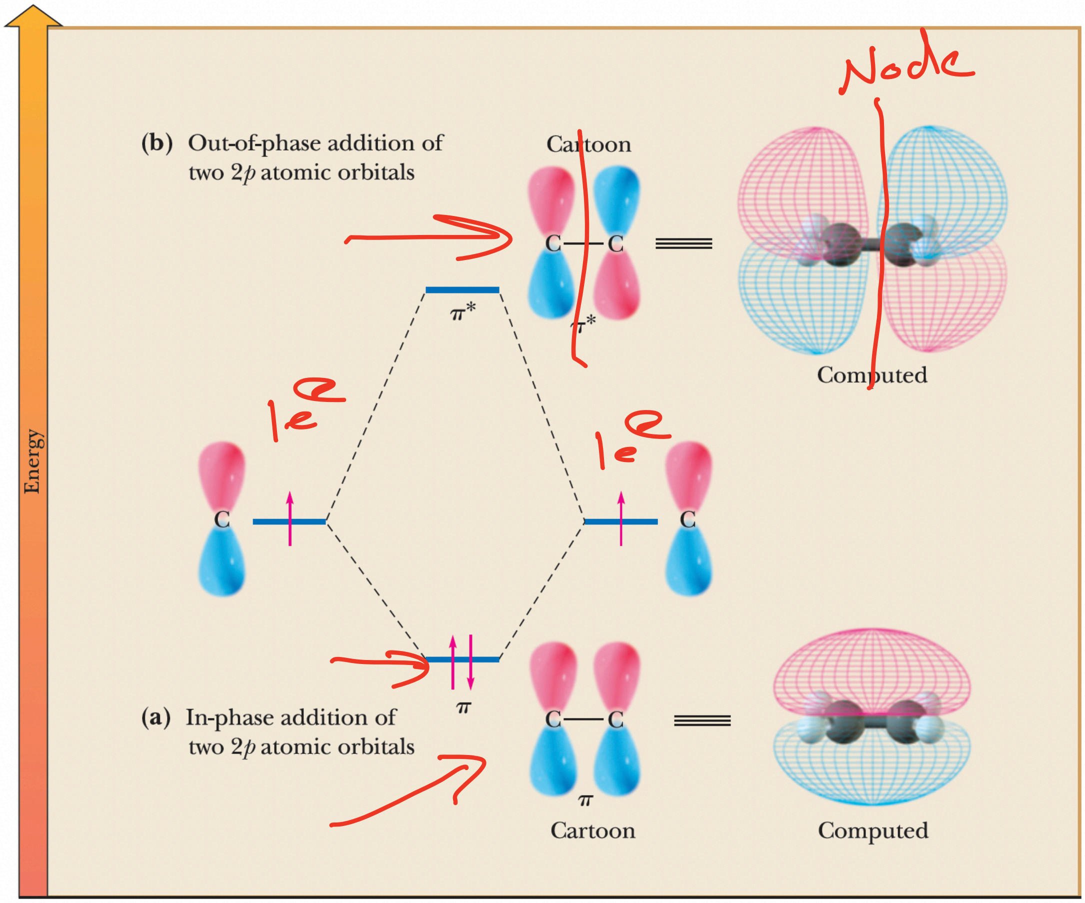
Like waves → orbitals can add constructively and destructively

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

→ Half of these are bonding molecular orbitals

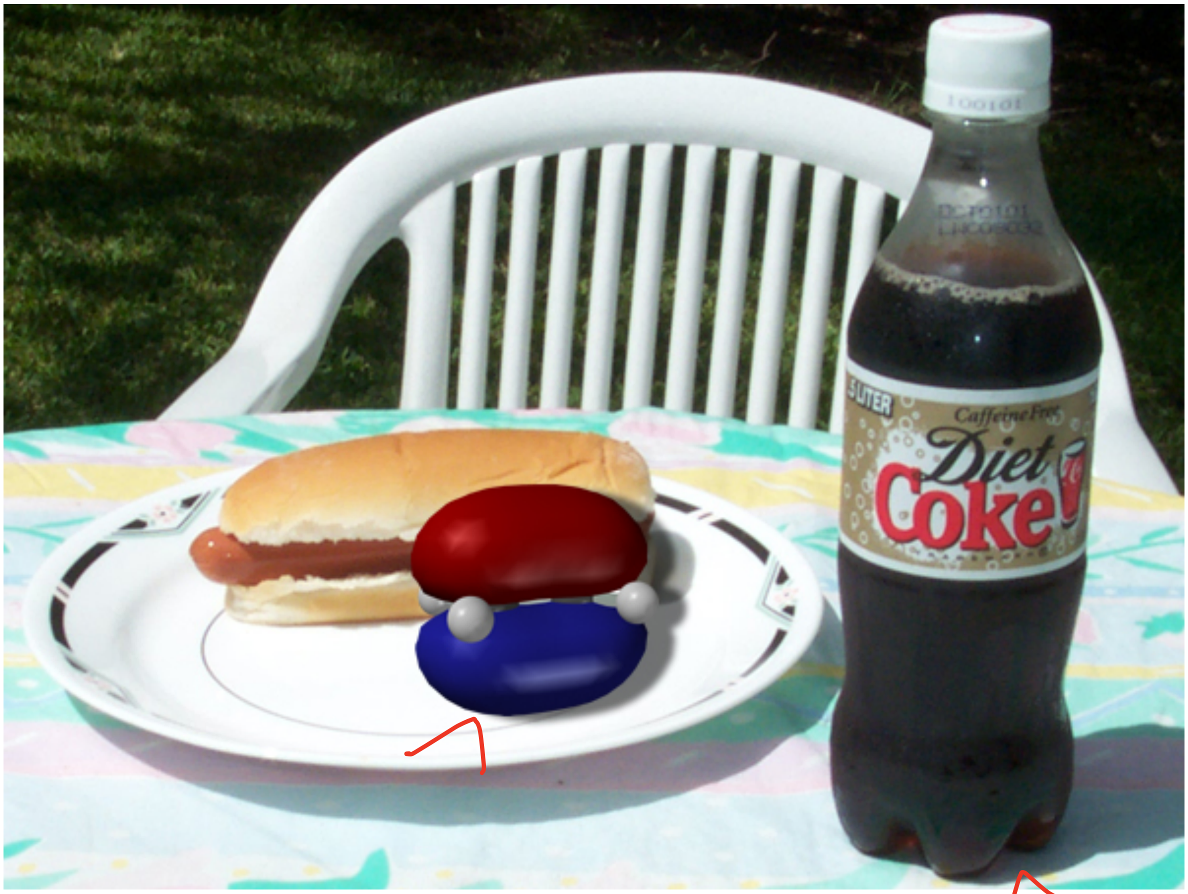
→ Half of these are antibonding molecular orbitals

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



Watch a video explanation

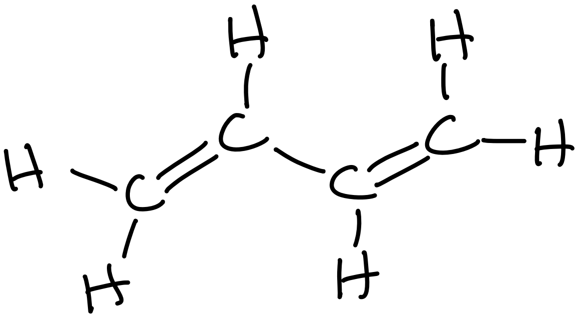
FIGURE 1.21 Molecular orbital mixing diagram for the creation of any C—C π bond. (a) Addition of two p atomic orbitals in phase leads to a π orbital that is lower in energy than the two separate starting orbitals. When populated with two electrons, the π orbital gives a π bond. (b) Addition of the p 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.



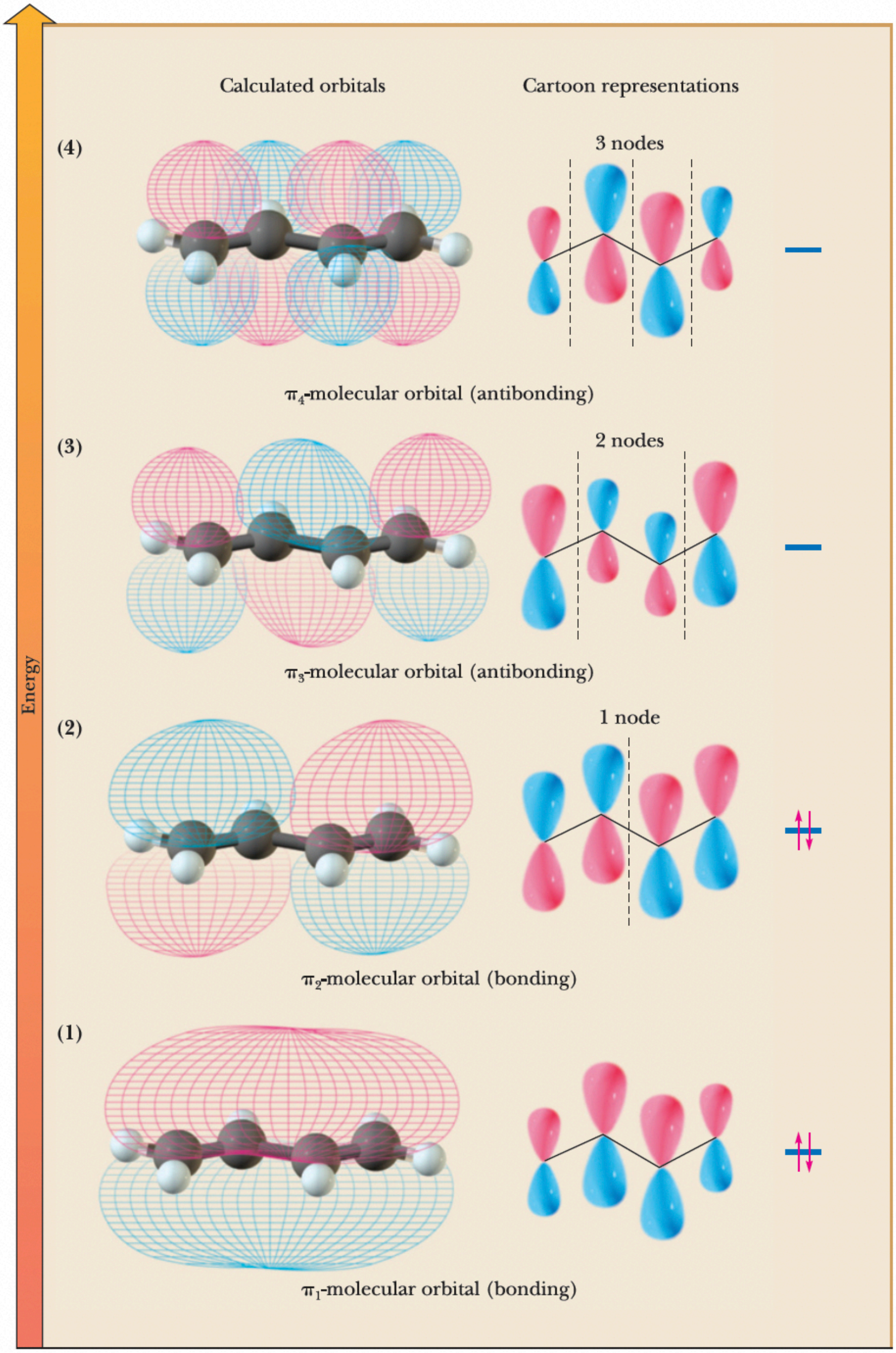
π bonding orbitals look like hot dog buns → formed from overlap of 2p orbitals
⇓
"to pee"

If you drink a lot of this you have 2 P!
(to pee)

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



1,3-Butadiene



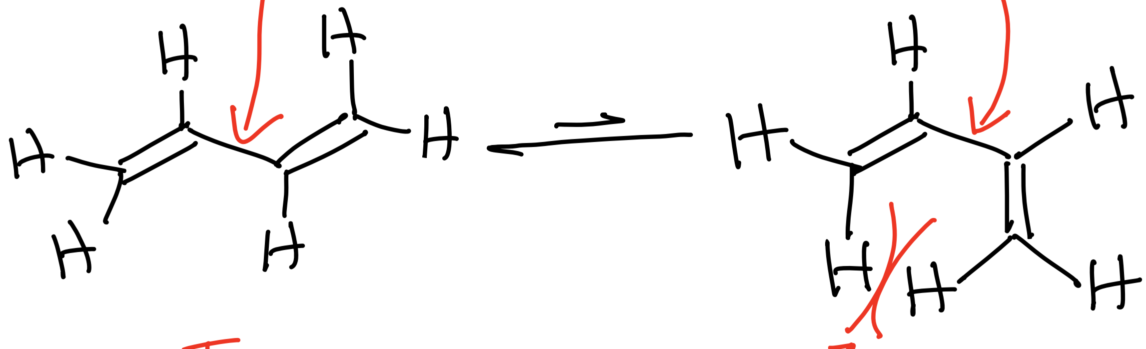
Watch a video explanation

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 two carbon atoms is not a normal sigma bond

→ Partial π bond

→ Does NOT rotate freely



s-Trans

Steric strain

s-Cis

More stable

Less stable due to some steric strain

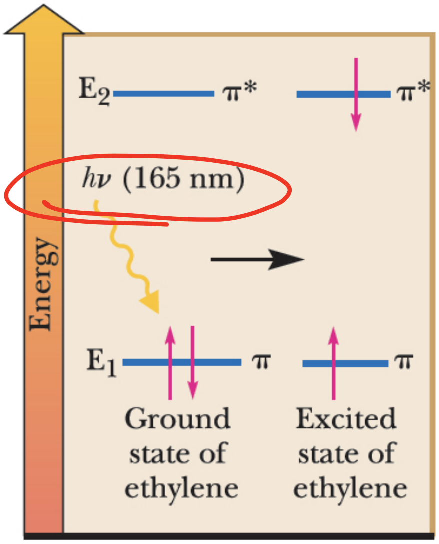


FIGURE 20.6 A $\pi \rightarrow \pi^*$ transition in excitation of ethylene. Absorption of ultraviolet radiation causes a transition of an electron from a π-bonding MO in the ground state to a π-antibonding MO in the excited state. There is no change in electron spin.

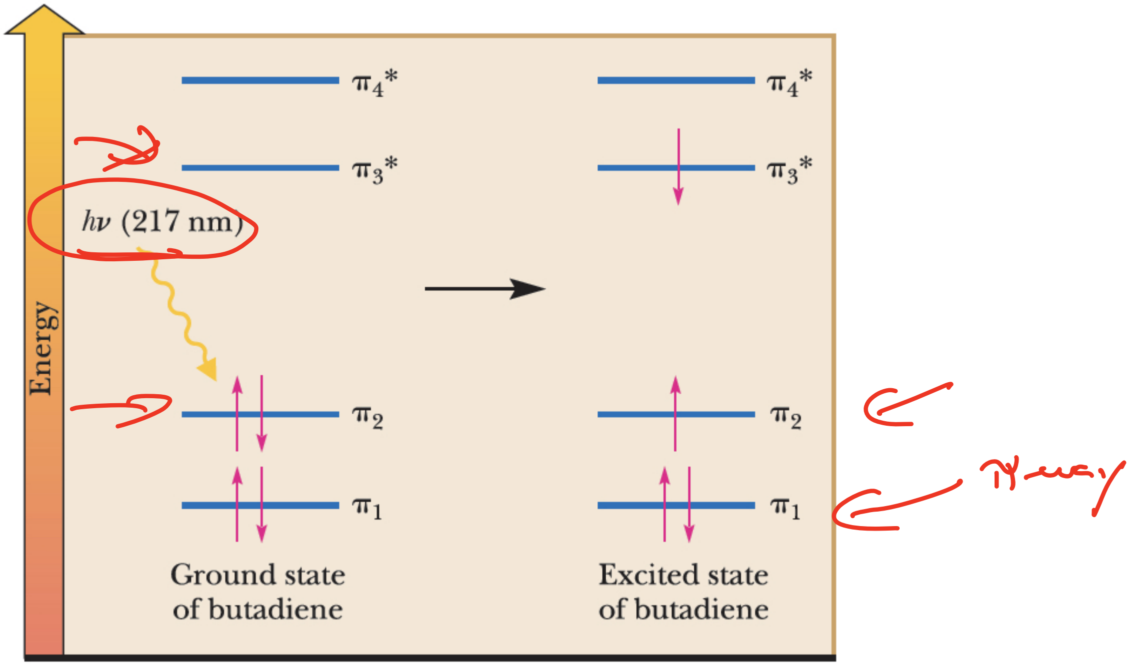


FIGURE 20.7 Electronic excitation of 1,3-butadiene; a $\pi \rightarrow \pi^*$ transition.

As you add 2p orbitals →
the energy gap between
the highest filled
π molecular orbital
and the lowest unfilled
π molecular orbitals
gets smaller ⇒ leads
to longer wavelength
of light photon of
the correct energy
to be absorbed.

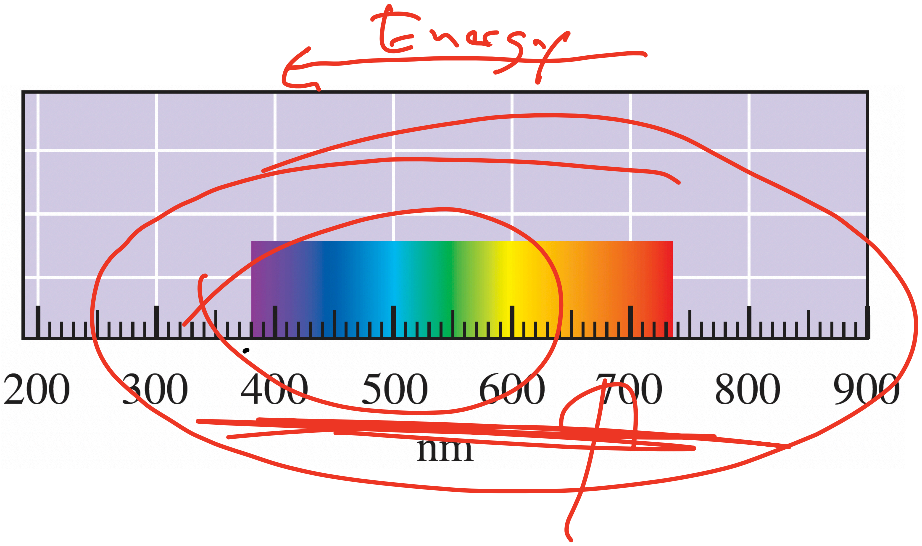
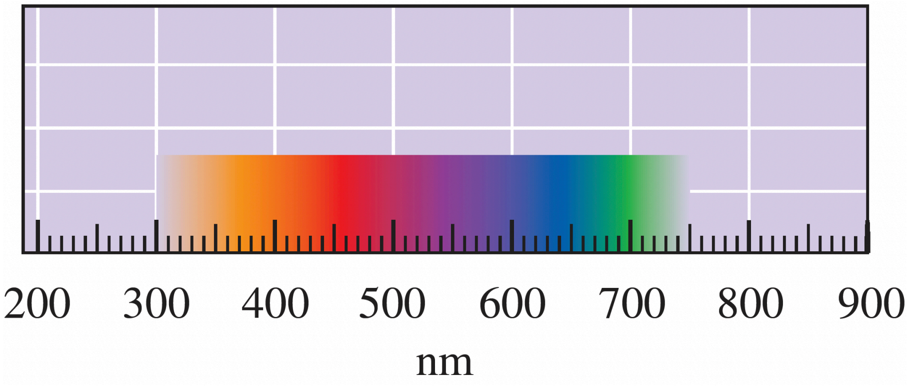
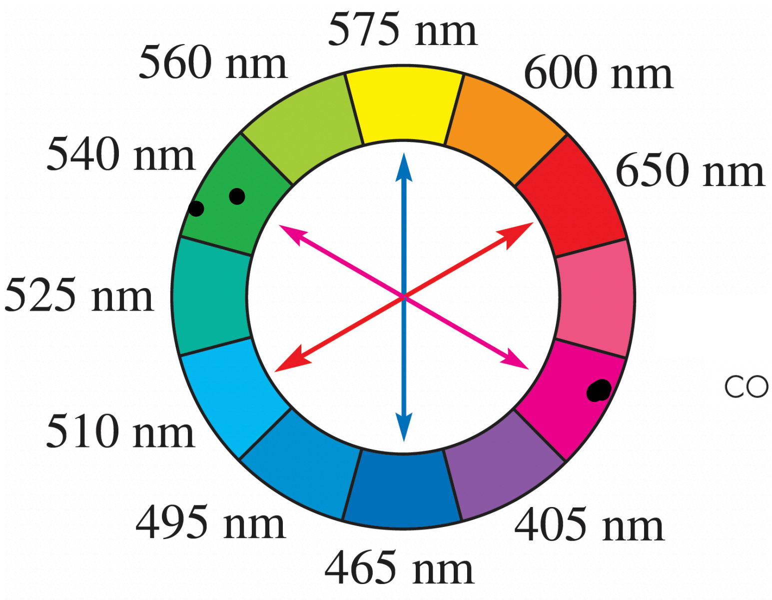


FIGURE 20.5 (a) Visible light color-wavelength correlation.



(b) Approximate color of substance (reflected light) if a single wavelength (i.e., the wavelength listed on the numerical scale of the *x*-axis) is absorbed.



(c) Complementary colors on a color wheel.

Colored arrows are complementary