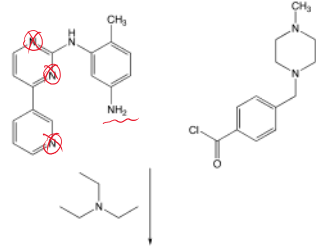


Week8 Handout

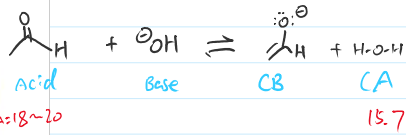


Gleevec – Novartis (\$4.65 Billion in sales in 2015). A kinase inhibitor that is a first of its kind pill capable of treating certain blood cancers with only limited side effects. It was designed to combat leukemias with the relatively common "Philadelphia chromosome" (BCR-ABL kinase gene fusion)

Weaker bases are favored at equilibrium

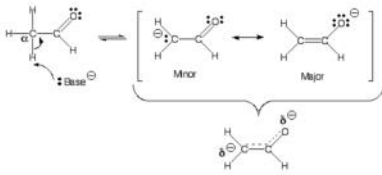
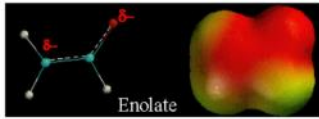
Compound	pKa
HCl	-7
Strongest Acid (Weakest conjugate base)	
Carboxylic acids [*]	3-5
p-Dicarbonyls [*]	10
p-Ketones [*]	11
p-Diesters [*]	13
Water	15.7
Alcohols	15-19
Acid chlorides [*]	16
Aldehydes [*]	18-20
Ketones [*]	18-20
Esters [*]	23-25
Terminal Alkynes	25
LDA	40
Terminal Alkanes	44
Alkanes	51
Weakest Acid (Strongest conjugate base)	

A) Reactions are favored (i.e. have a positive ΔG) if they lead to formation of a weaker acid and/or weaker base.
 B) Checking pKa values can predict if a reaction has a positive even if there are other steps besides a proton transfer.
 C) Recall that the conjugate base of a stronger acid (lower pKa) is a weaker base.
 D) Check the pKa of the conjugate acid of the base on either side of the equilibrium. Lower pKa value indicates a stronger conjugate acid (lower pKa value) will be the weaker base and will be favored at equilibrium.
 E) Another way to look at it is that the base that is formed at equilibrium is the one that has the more stabilized anion, i.e. the one with the larger spread around more (electronegative) atoms.
 F) Above is a pKa table that we will refer to often.



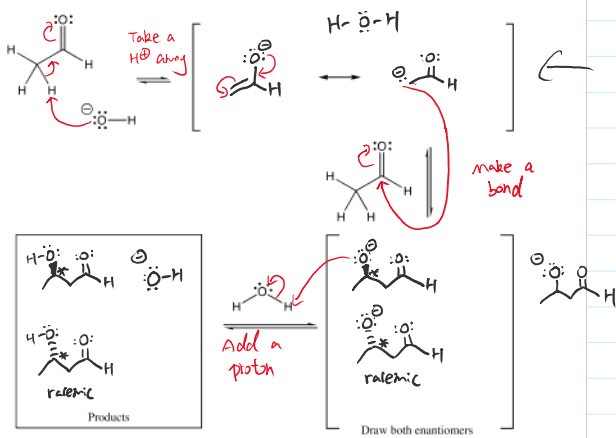
^{*}These have resonance stabilized anions

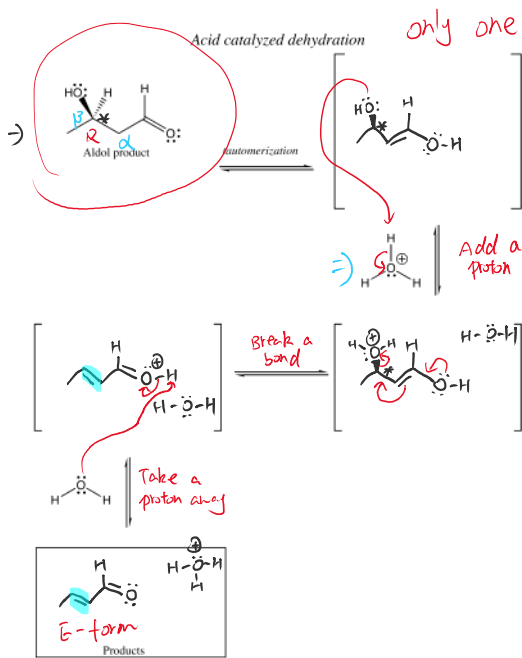
Enolates as nucleophiles



- A) Enolates are resonance stabilized, with a partial negative charge on carbon and oxygen.
- B) Enolates are nucleophiles, so they could react at either the carbon atom or oxygen atom. The partial negative charges give them the **opportunity** to react at either the carbon or oxygen.
- C) Reaction at the carbon atom gives the final product a C=O bond, while reaction at the oxygen atom gives the final product a C=C bond. However, C=O bonds are stronger than C=C bonds, so the **motive is to react at the carbon atom with most electrophiles.**

Aldol Reaction \rightarrow Catalytic in base





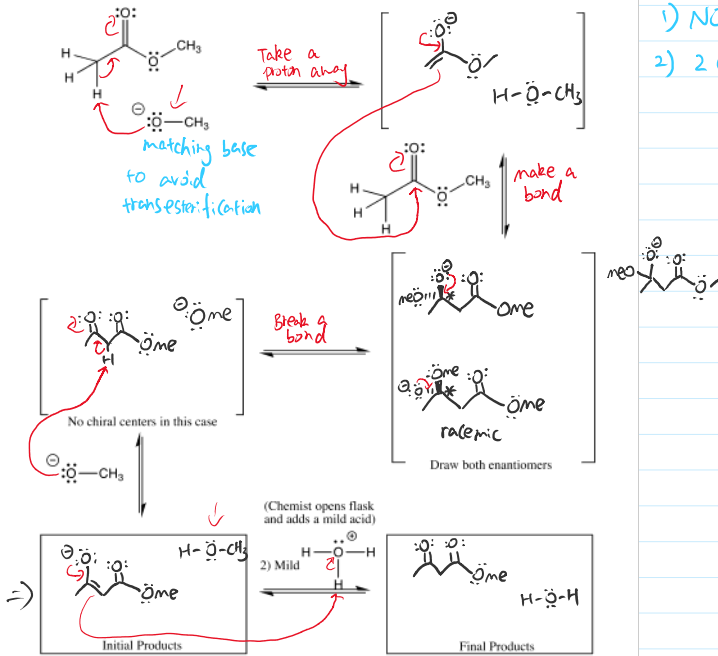
Mixed Aldol: between aldehyde and ketone.



Why Aldol does not work w/ ketones alone:



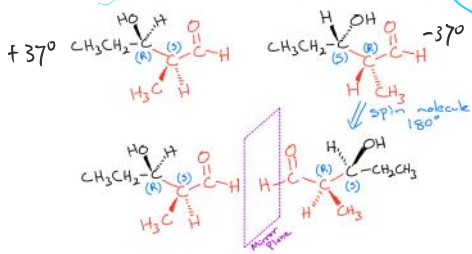
Claisen Condensation → Aldol w/ esters



1) NOT catalytic in base!

2) 2 esters require 1 equiv base

Enantiomers or Diastereomers? at least two chiral centers

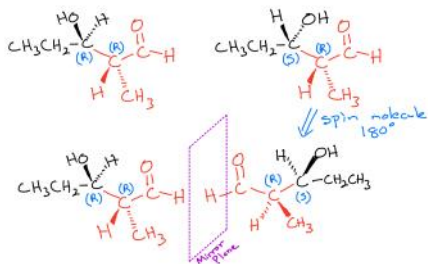


describes types of stereoisomers

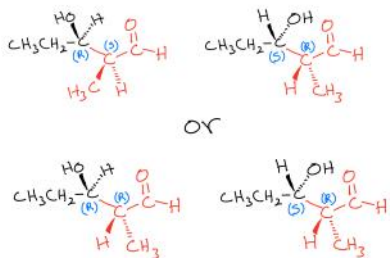
"racemic" = concentration-related:
have 1:1 mixture of enantiomers

plane-polarized light:

enantiomers will rotate the
plane-polarized light to the opposite
direction, but to the same amount.

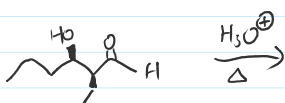


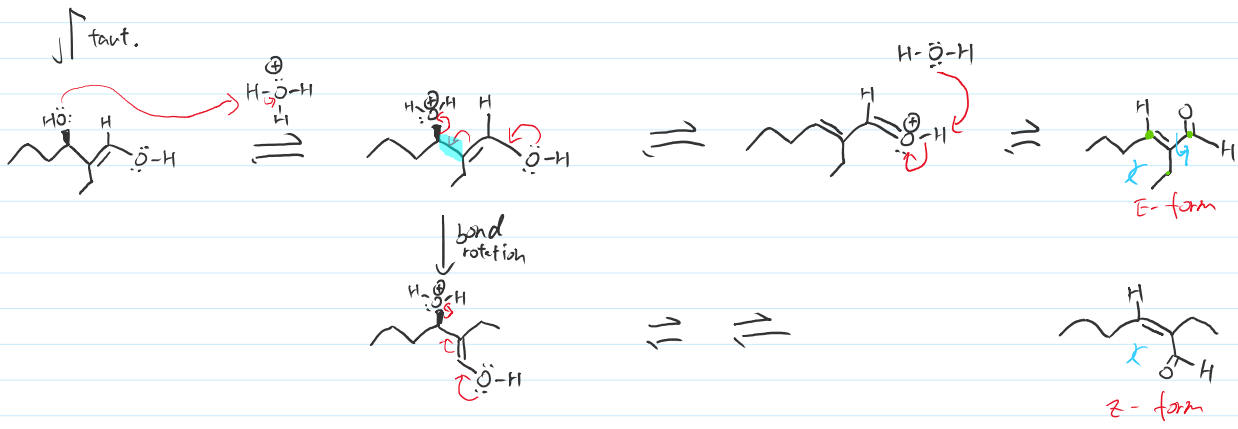
Which pair of molecules
could be a racemic mixture?



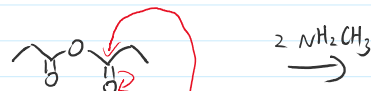
midterm practice:

p9, box 2

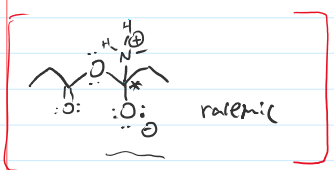




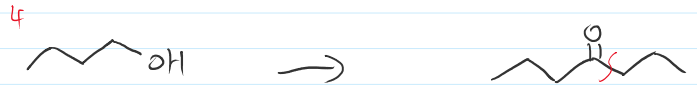
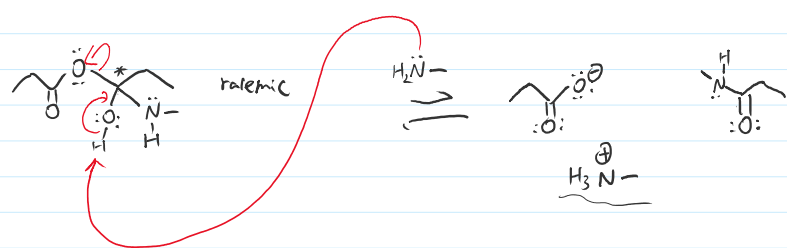
P8, box 1



↑ $\text{H}_2\text{N}-$



↑ proton transfer



- ① ozonolysis → alkene
- ② decarboxylation → CCCCCOH
- ③ Haloforn formation → CCCCBr

(requires at least 1 methyl group on the ketone)

