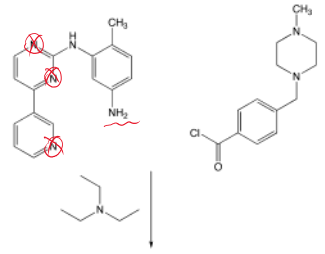
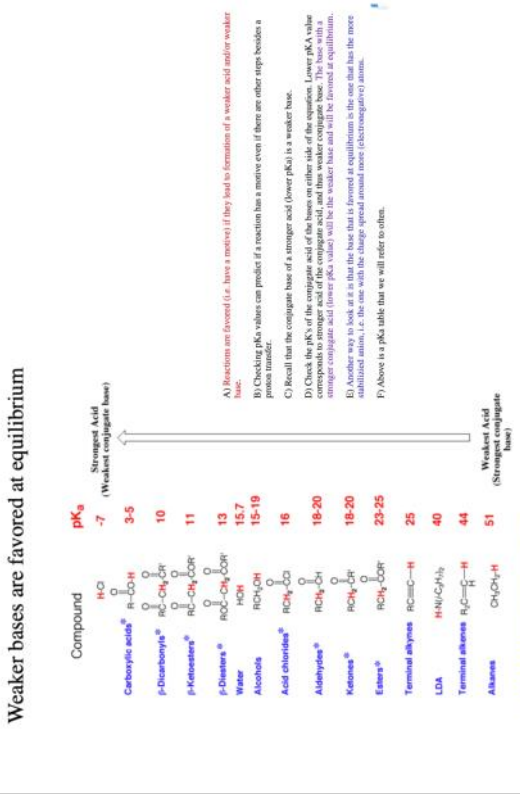
MTW8: 3-6

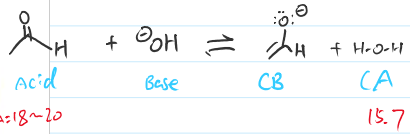
2023年3月6日 14:45

Week8 Handout

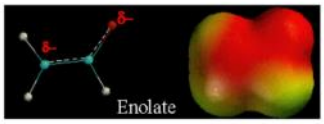


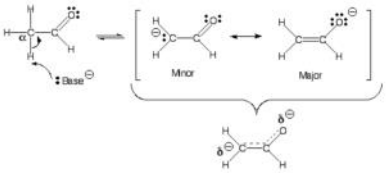
Gleevec – Novartis ($4.65 Billion in sales in 2015). A kinase inhibitor that is a first of its kind pill capable of treating certain blood cancers with only limited side effects. It was designed to combat leukemias with the relatively common "Philadelphia chromosome" (BCR-ABL kinase gene fusion)





Enolates as nucleophiles



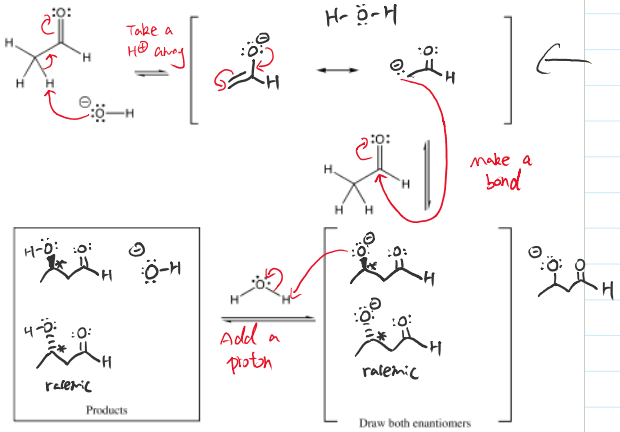


A) Enolates are resonance stabilized, with a partial negative charge on carbon and oxygen.

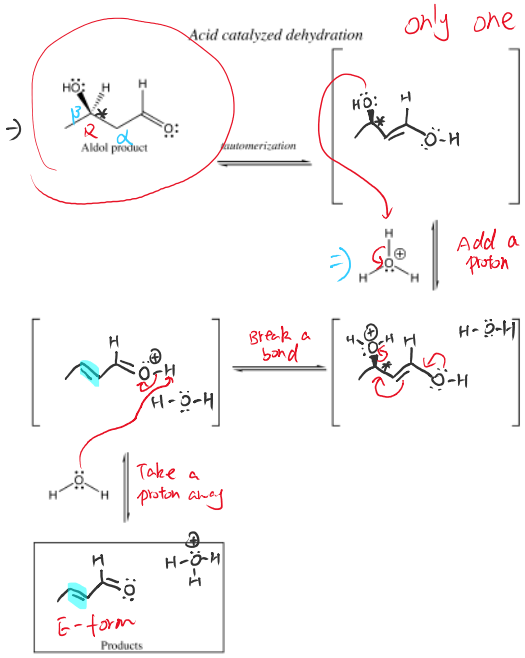
B) Enolates are nucleophiles, so they could react at either the carbon atom or oxygen atom. The partial negative charges give them the **opportunity** to react at either the carbon or oxygen.

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.

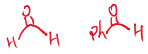
Aldol Reaction → Catalytic in base



only one that forms E as major pdt.

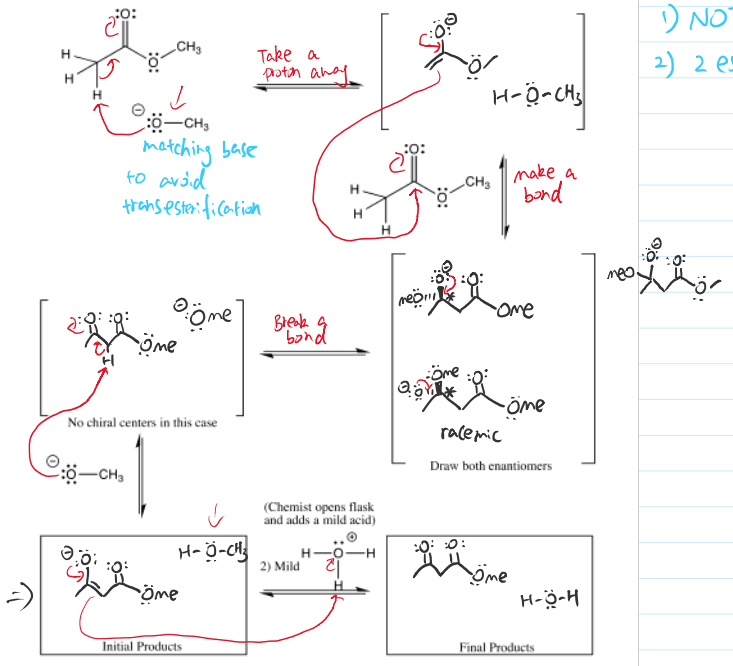


mixed Aldol : between aldehyde and ketone.



why Aldol does not work w/ ketones alone:

Claisen Condensation → Aldol w/ esters

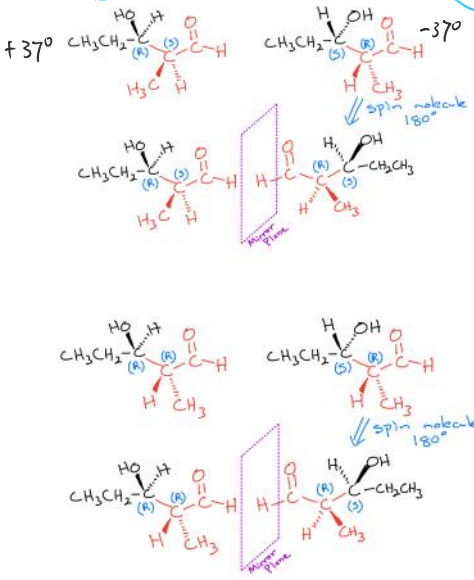


1) NOT Catalytic in base!
2) 2 esters require 1 equiv base

Enantiomers or Diastereomers?

at least two chiral centers

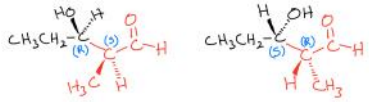
describes types of stereoisomers



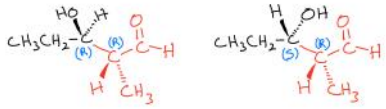
"racemic" = concentration-related:
have 1:1 mixture of enantiomers

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?



or



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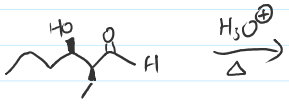
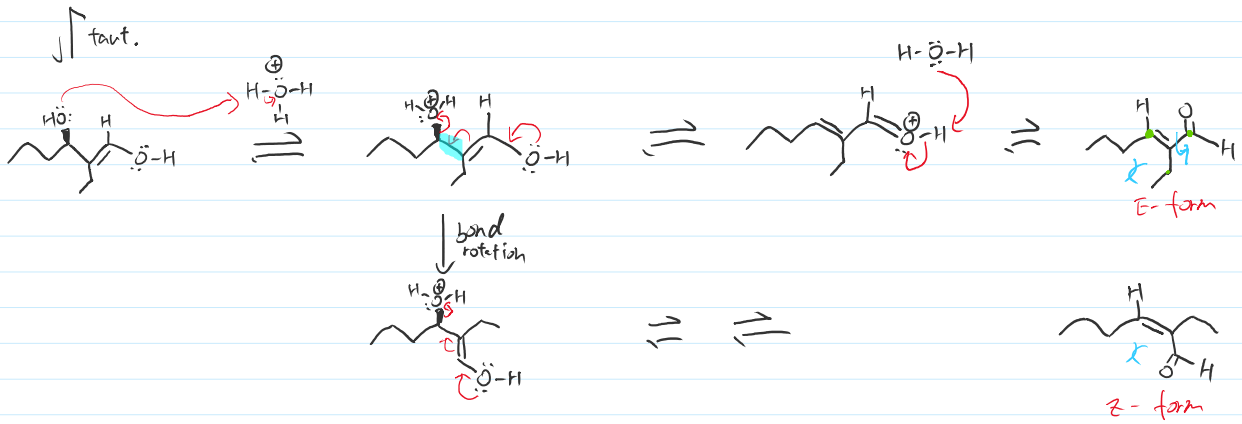
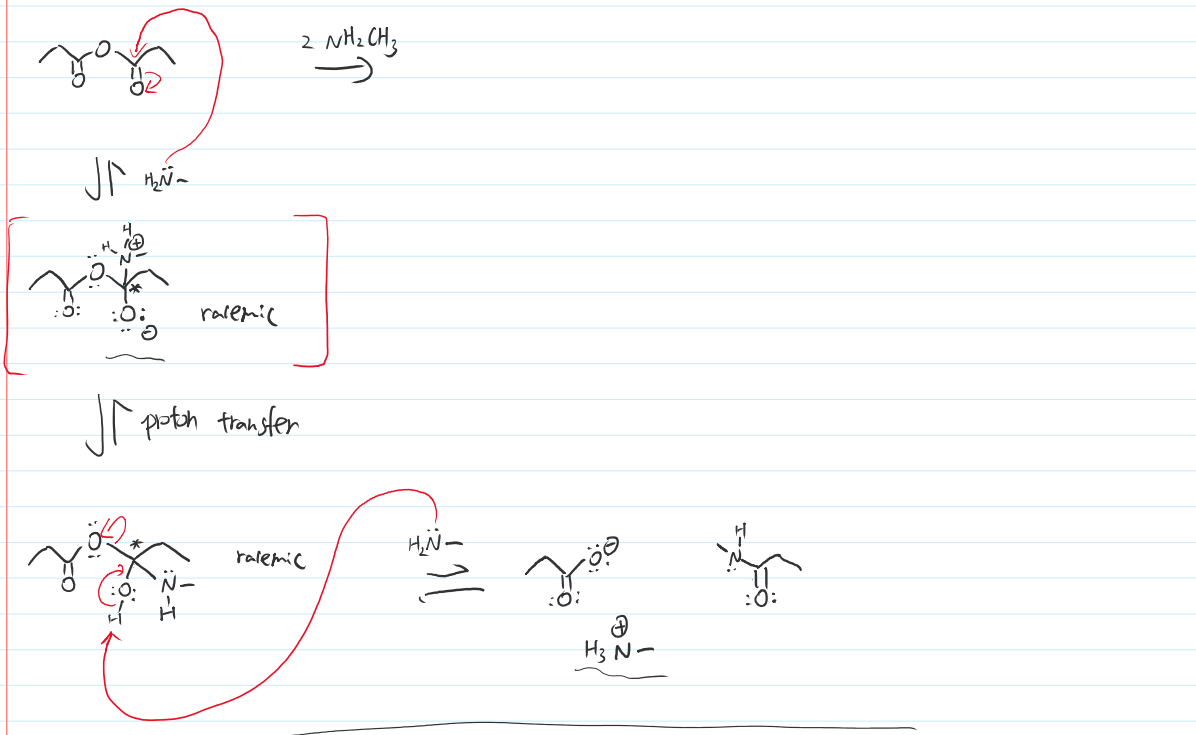
midterm practice:

p9, box2





P8, box 1



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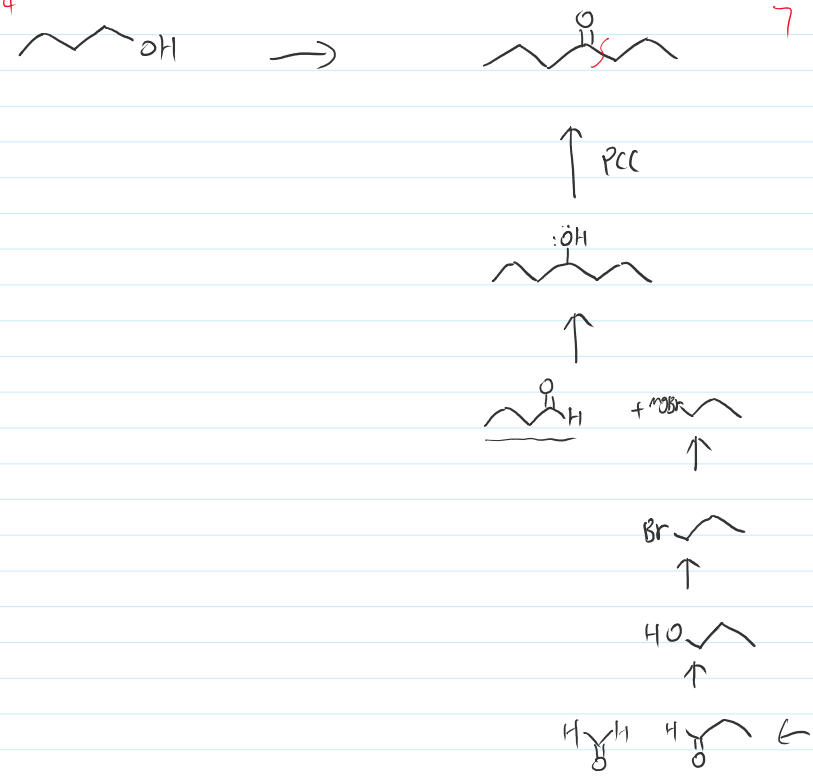

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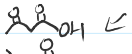
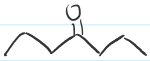
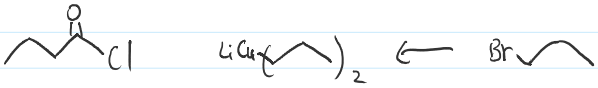
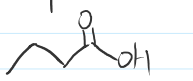
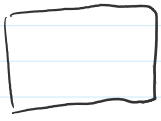
① Ozonolysis → alkene
② decarboxylation → 
③ Haloform formation → 
(requires at least 1 methyl group on the ketone)







1) 1 eq NaOH
2) $H_3O^{\oplus}$



$HA + {}^{\ominus}OH \rightleftharpoons H\text{-}O\text{-}H + A^{\ominus}$ pKa = 15.7

$HA + {}^{\ominus}OMe \rightleftharpoons H\text{-}OMe + A^{\ominus}$ pKa = 17

0.5 eq NaOH

β-keto ester (deprotonated) + H_2O → β-keto ester + 0.5 equiv $^{\ominus}OH$

Initial Pdt