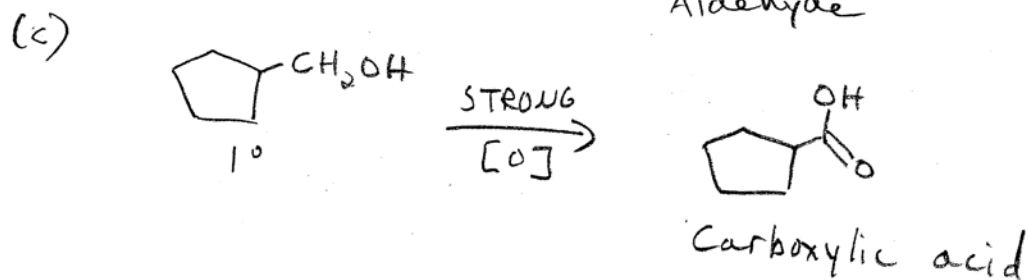
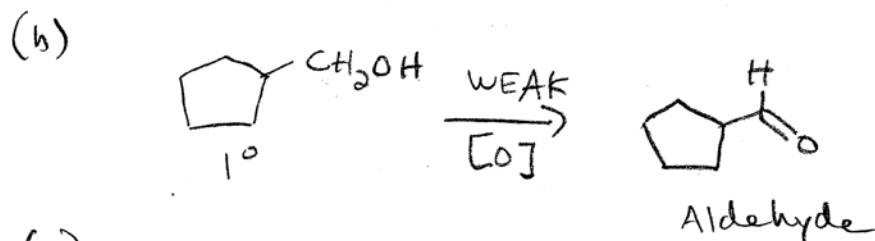
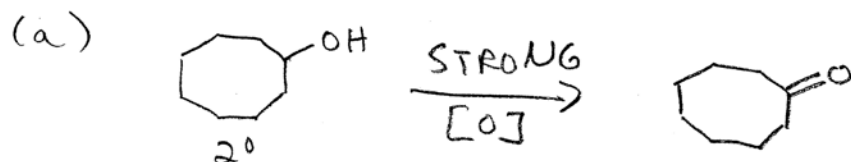


# Problem Set #6 Key

①

13.12

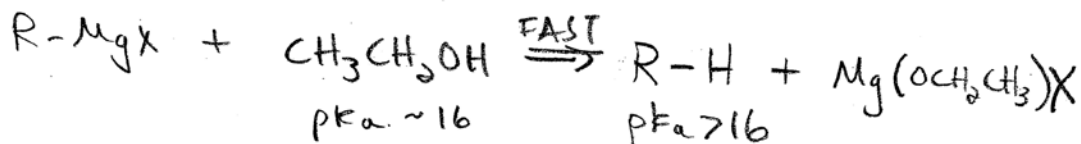
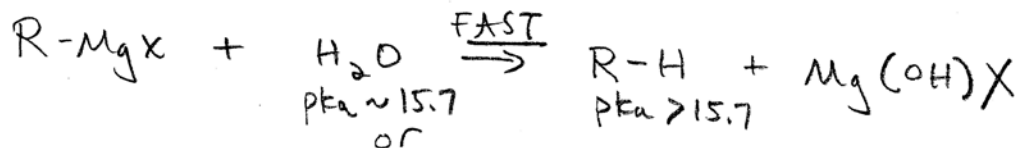


13.19

Grignard reagents of the form

$R-MgX$  can be treated as " $R^-$ "

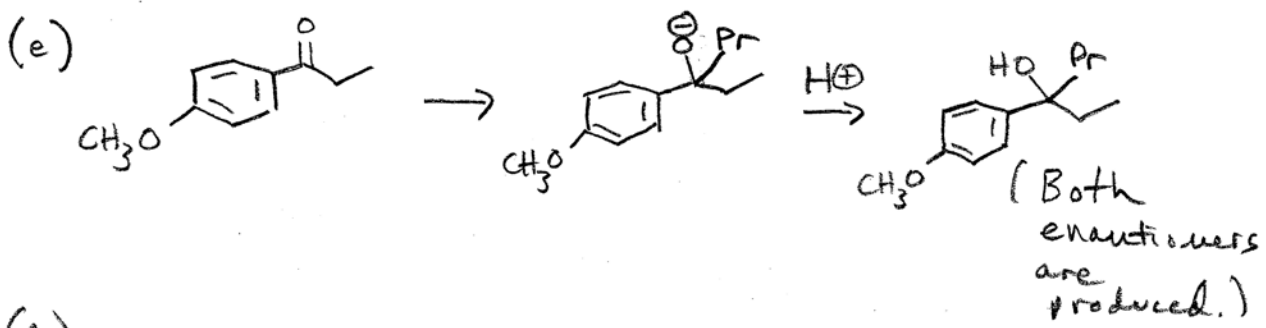
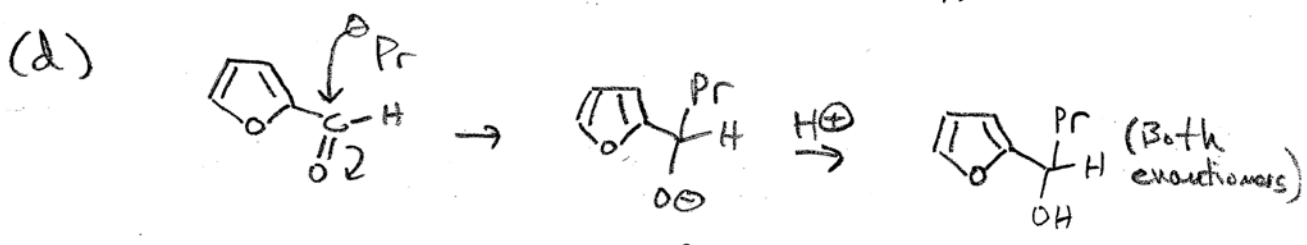
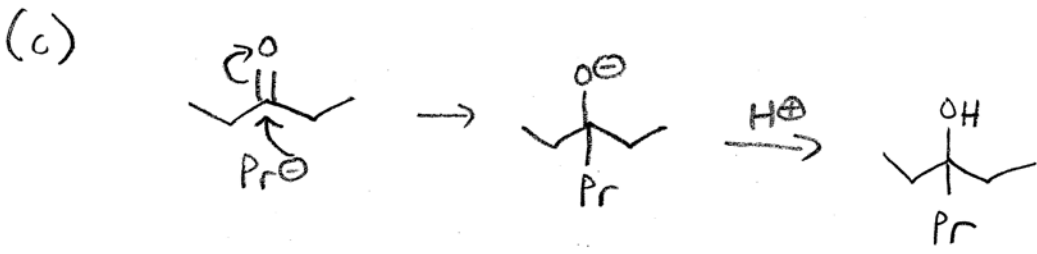
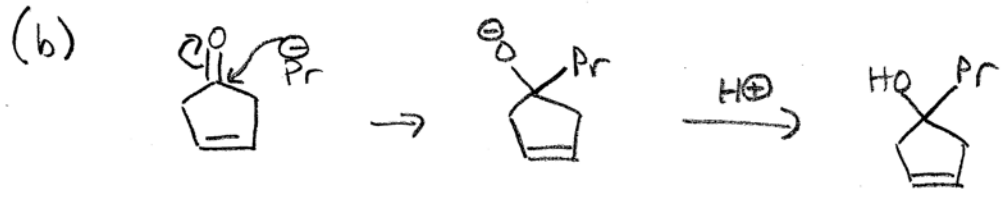
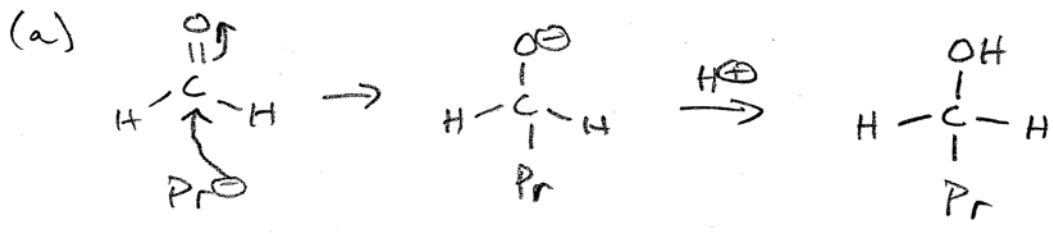
which are very strong bases! (high  $pK_a$  of acidic form)  
so the acid-base reaction predominates:



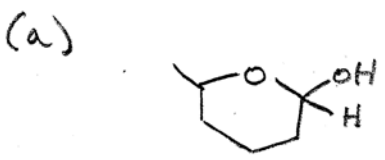
The Grignard reagent reacts w/ these hydroxylated compounds rather than with the desired target carbonyl compound.

13.20

Propyl magnesium bromide is  $\text{CH}_3\text{CH}_2\text{CH}_2\text{MgBr}$  or  $\text{PrMgBr}$  or " $\text{Pr}^\ominus$ "

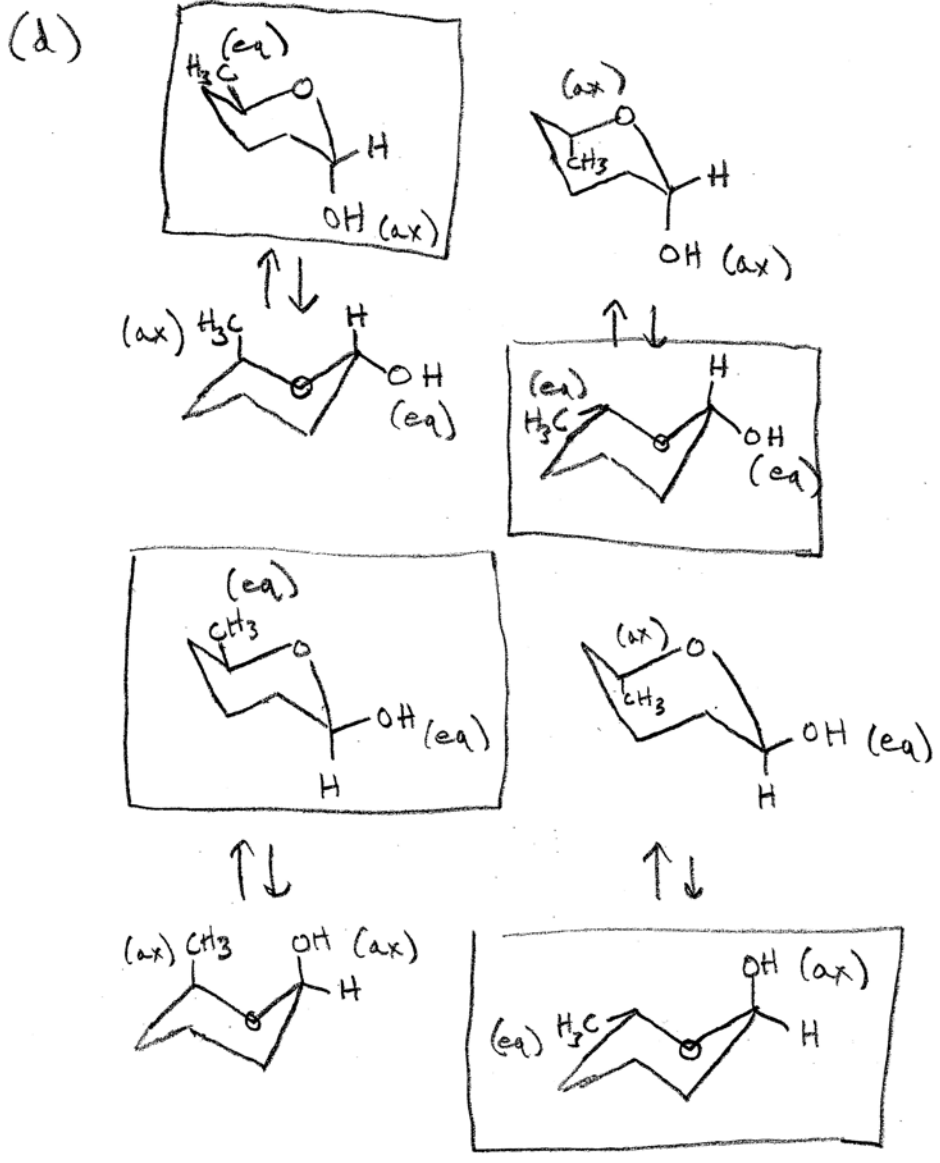


13.22



(b) 1 stereocenter in 5-hydroxyhexanal = 2 stereoisomers (enantiomers)

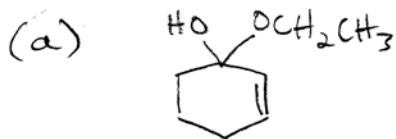
(c) 2 stereo centers = 4 stereoisomers



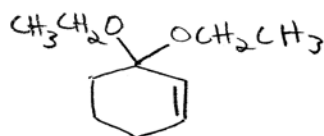
(e) The boxed isomers are more stable, assuming diaxial interactions play a larger role than anomeric effects (see me for an explanation of the latter.)

13.23

4

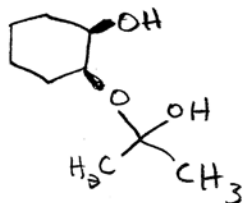


hemiacetal  
("hemiketal"  
is more  
correct)

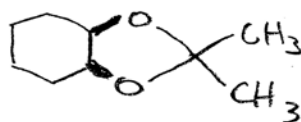


acetal  
("ketal"  
is more  
correct)

(b)

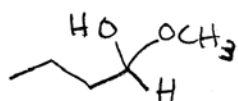


hemiacetal  
("hemiketal"  
is more correct)

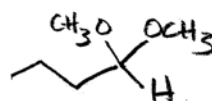


acetal  
("ketal" is  
more correct!)

(c)

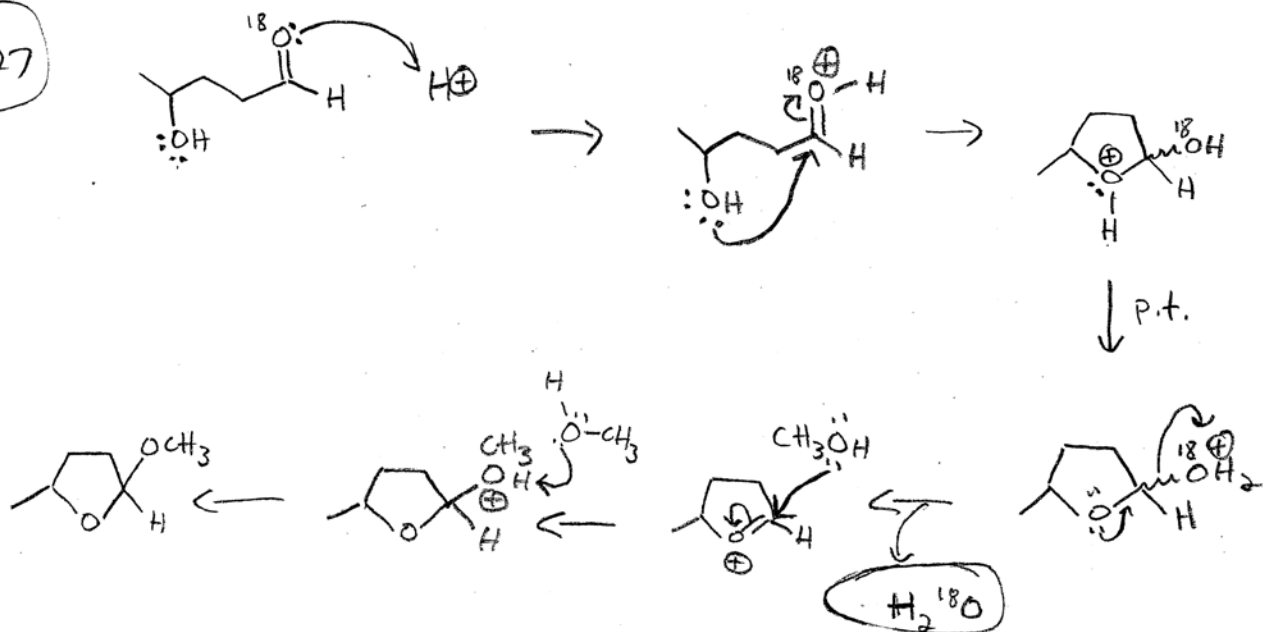


hemiacetal



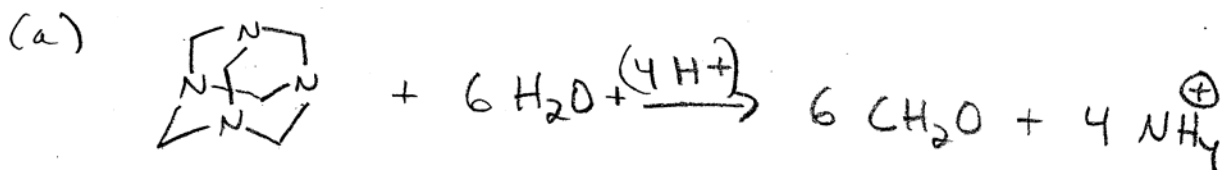
acetal

13.27



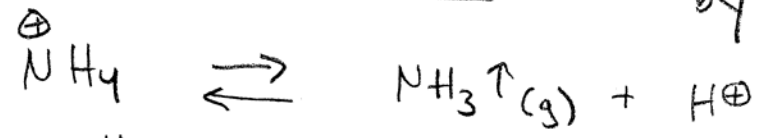
The O-18 label appears in the water,  
not in the acetal.

13.32



(b) NH<sub>4</sub><sup>+</sup> is a weak acid; under already acidic conditions (the kidneys) it would stay NH<sub>4</sub><sup>+</sup> so no change in pH would be expected.

In neutral aqueous media, the NH<sub>4</sub><sup>+</sup> would liberate some H<sup>+</sup> by



so the pH would begin to drop.

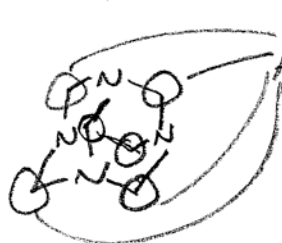
(c) "Nitrogen analog" means that nitrogens are substituted for other heteroatoms (such as O, S, P, etc.)

An acetal is  $\begin{matrix} \text{R} & \text{O} & \text{R} \\ & \diagdown & / \\ & \text{C} & \\ & / & \diagdown \\ \text{R} & & \text{H} \end{matrix}$  ∴ the

"nitrogen analog" is  $\begin{matrix} \text{R}_2\text{N} & & \text{NR}_2 \\ & \diagdown & / \\ & \text{C} & \\ & / & \diagdown \\ \text{R} & & \text{H} \end{matrix}$

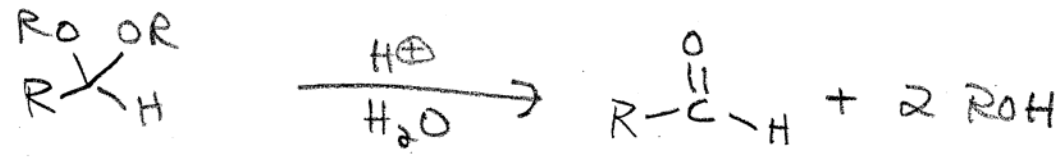
(Both N's bonded to the same C)

∴ methanamine is a nitrogen analog.

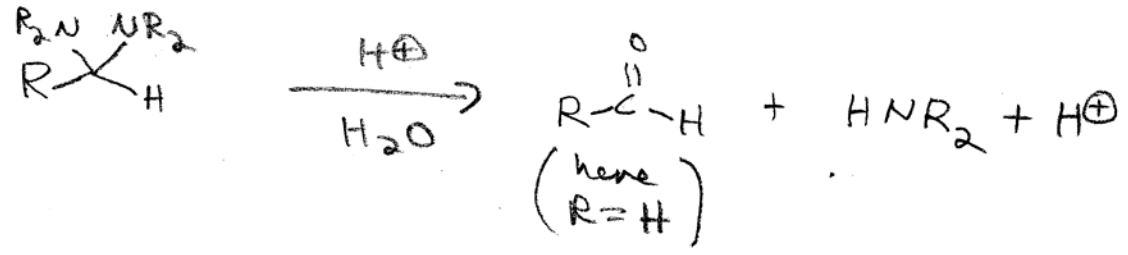


All have 2 N's attached as NR<sub>2</sub>! (6)  
 All C's participate in a nitrogen analogue of an acetal.

(d) The reaction of an acetal in acidic aqueous conditions is

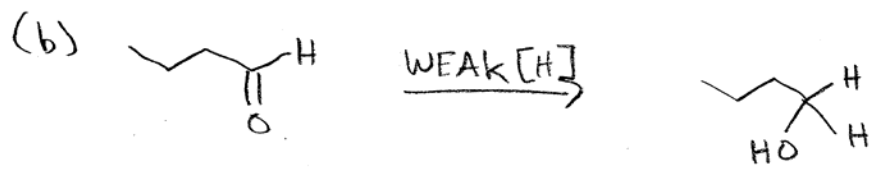
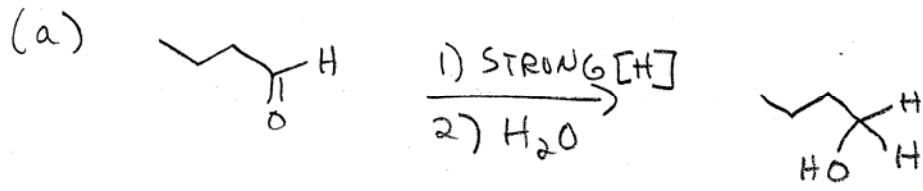
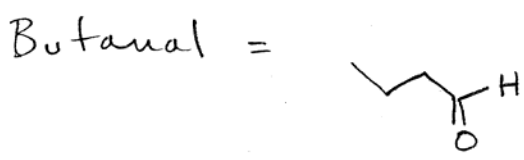


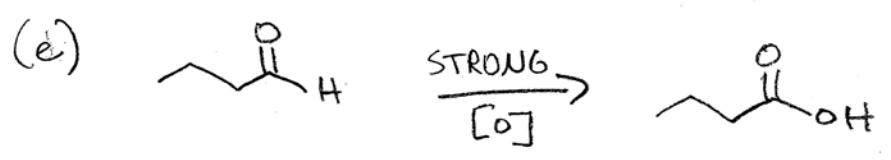
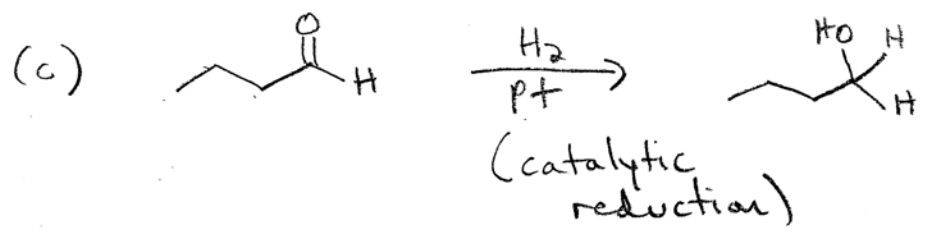
∴ the "nitrogen analog" is expected to act the same way:



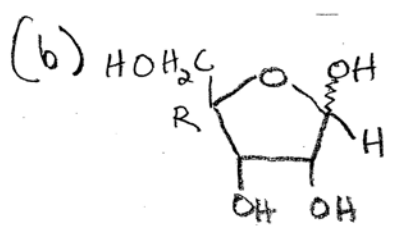
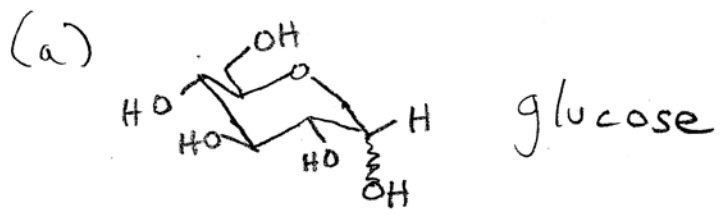
∴ methanamine breaks up in the acidic urinary tract!

13.35



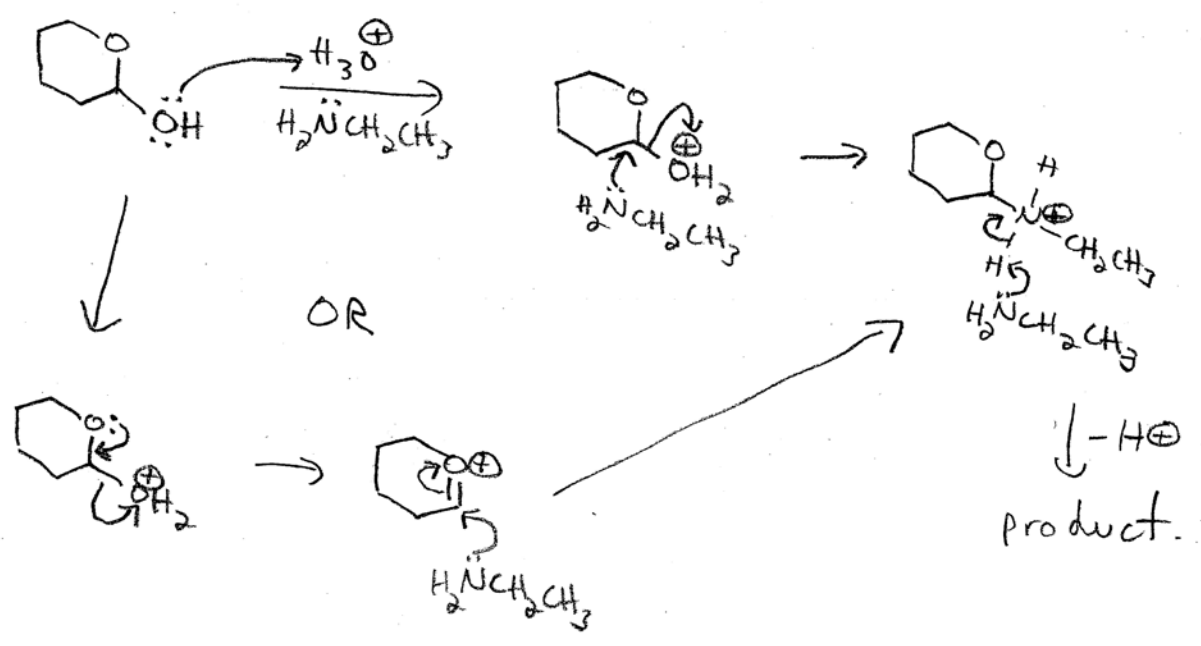


13.51



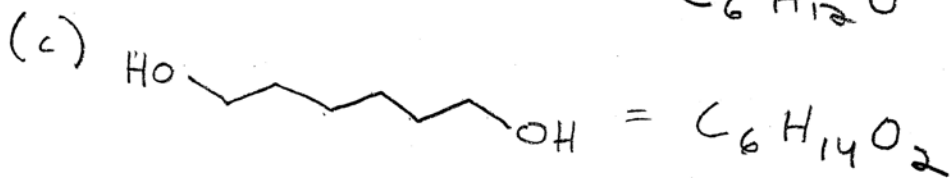
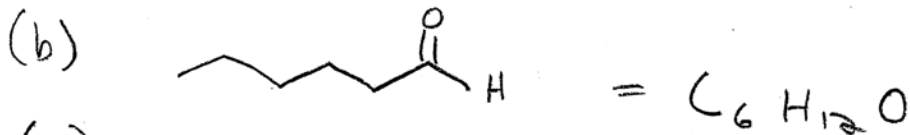
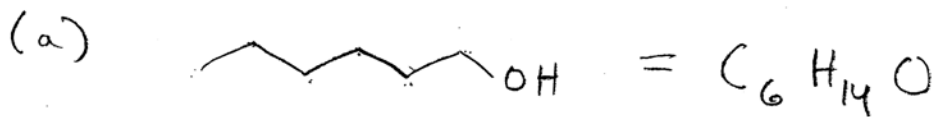
Building models helps!

13.52

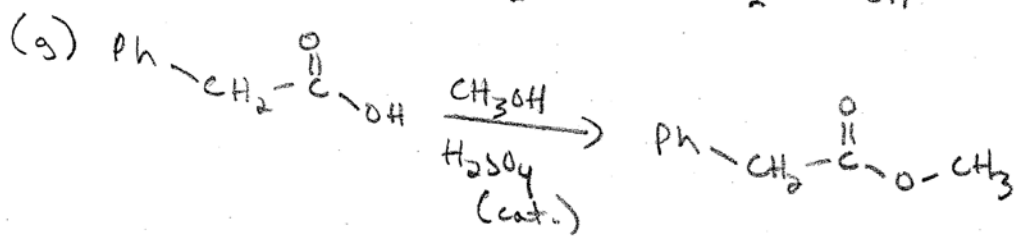
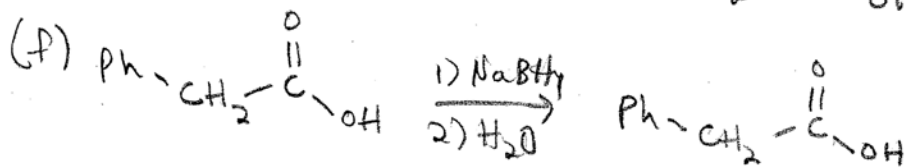
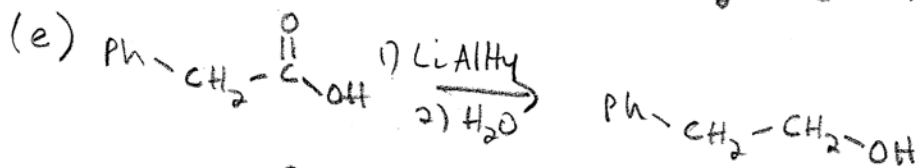
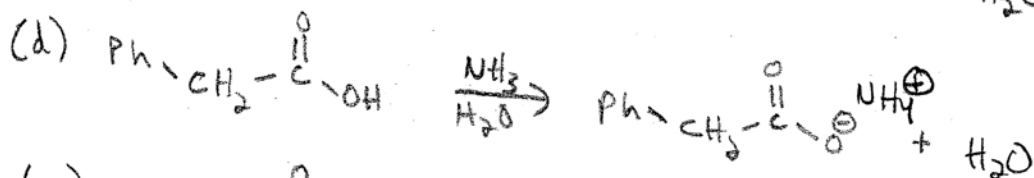
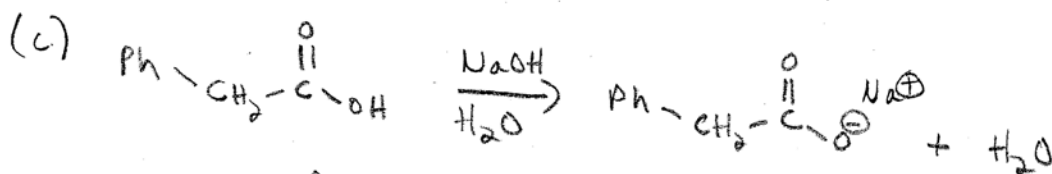
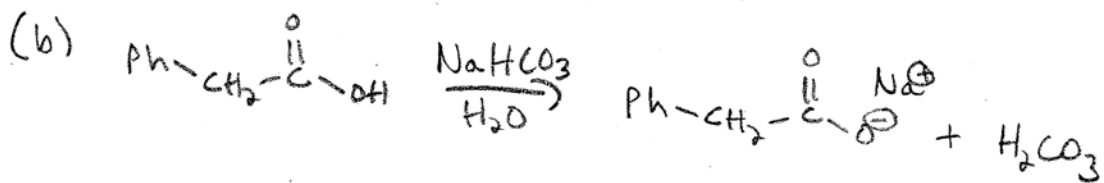
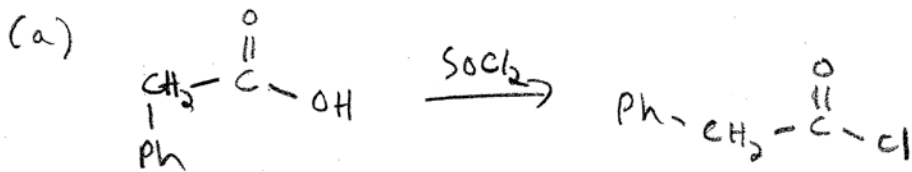


4.18

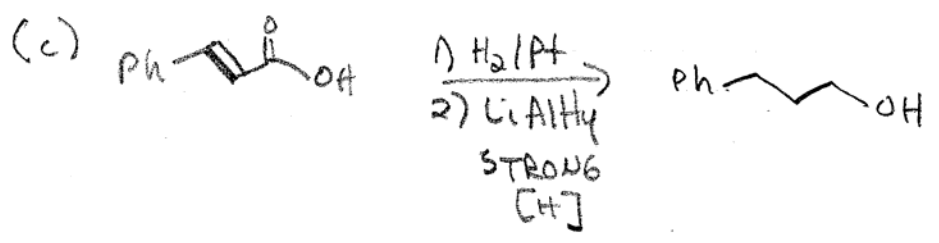
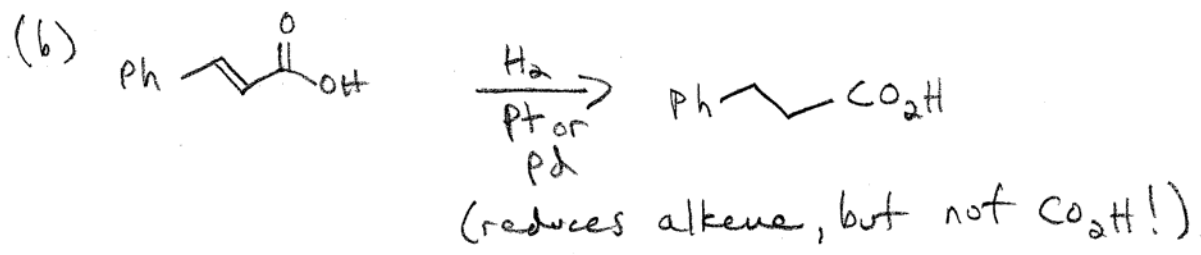
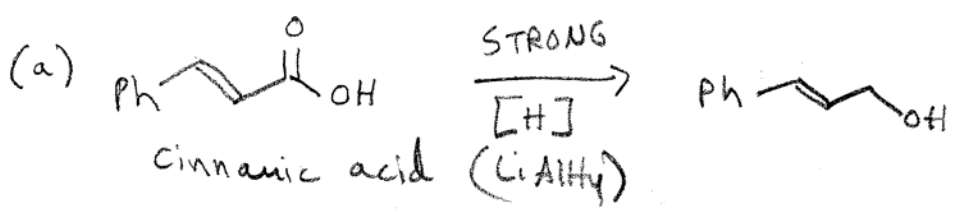
8



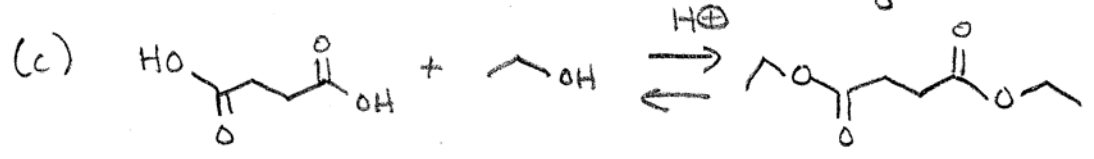
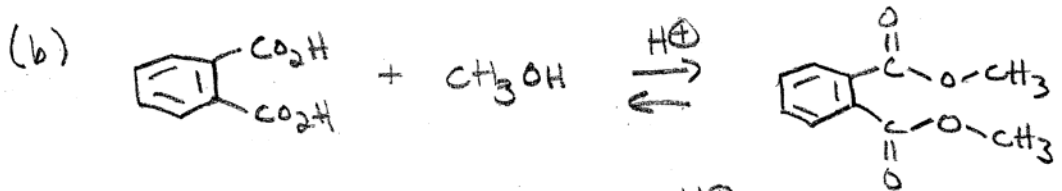
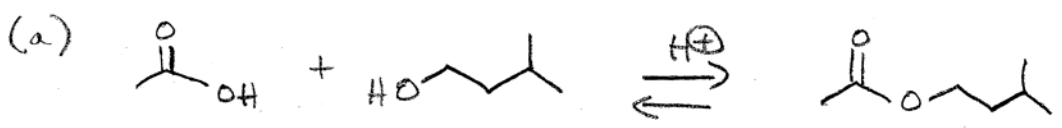
4.29



14.30

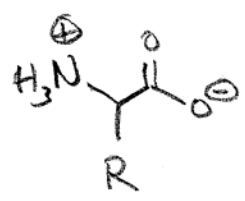


14.32



14.46

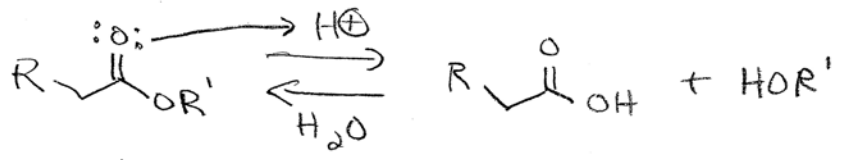
Inductive effect!! At physiologic pH,



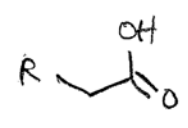
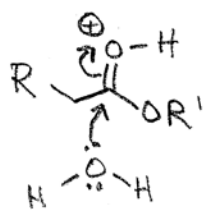
The positively charged  $\text{NH}_3^+$  group removes  $e^-$  density from the base, the  $\text{COO}^-$  group thereby stabilizing it.

More stable conjugate base = more acidic acid!

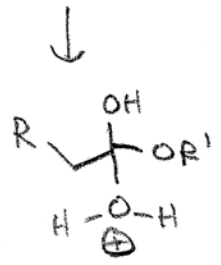
14.48



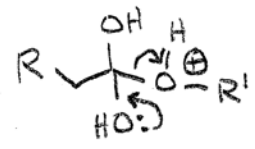
↓ protonation



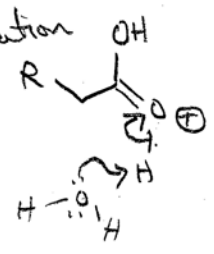
↑ -H<sup>+</sup>



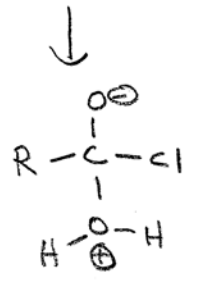
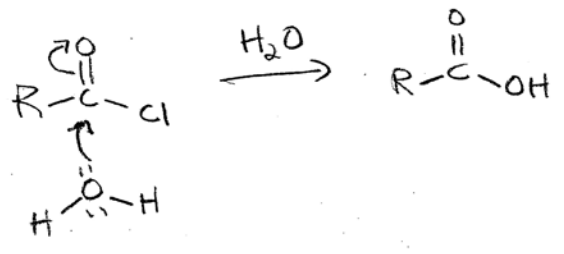
proton transfer



elimination

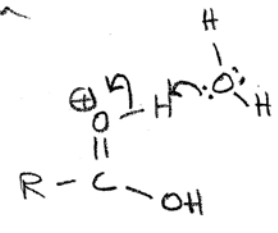
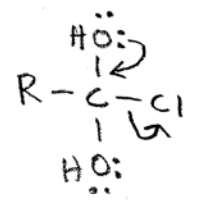


14.50

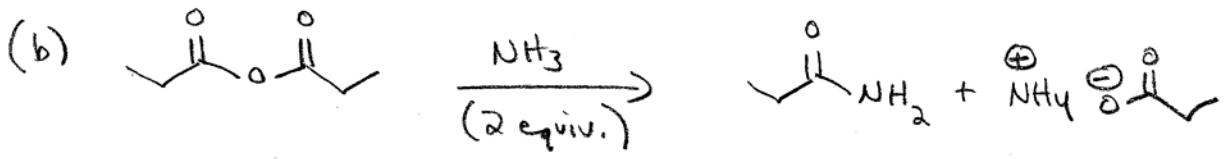
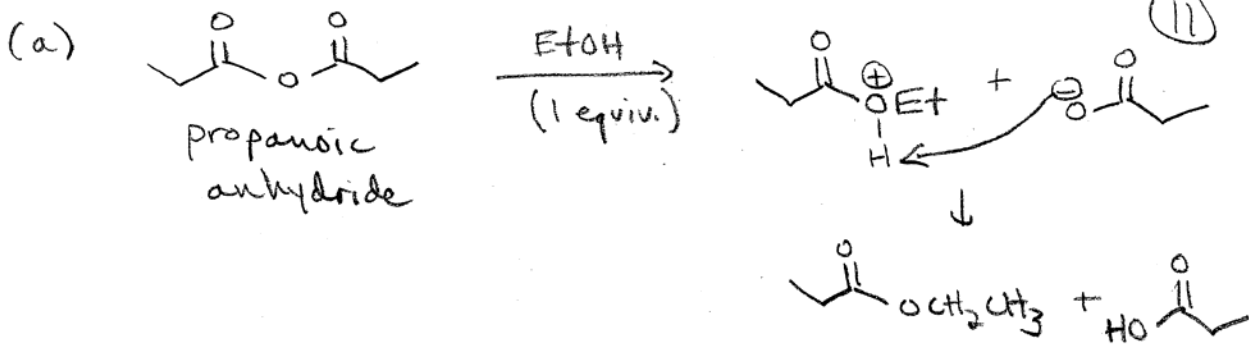


↓ proton transfer

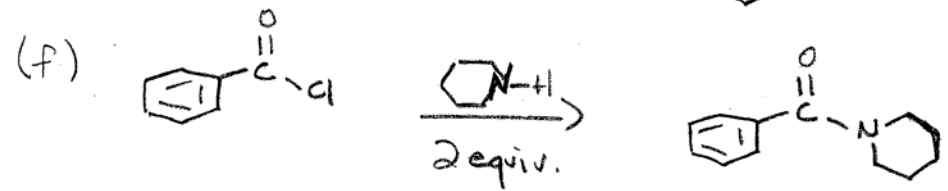
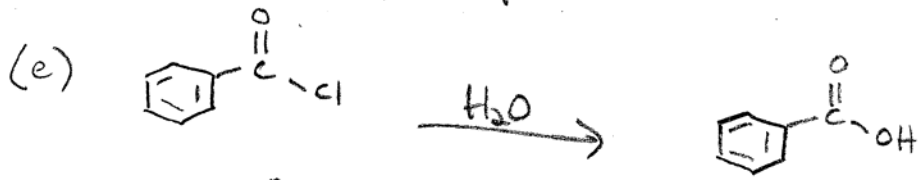
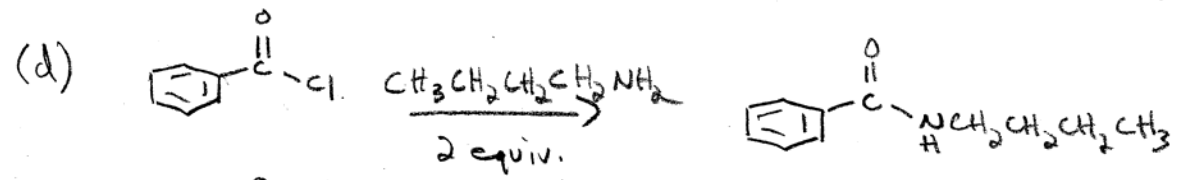
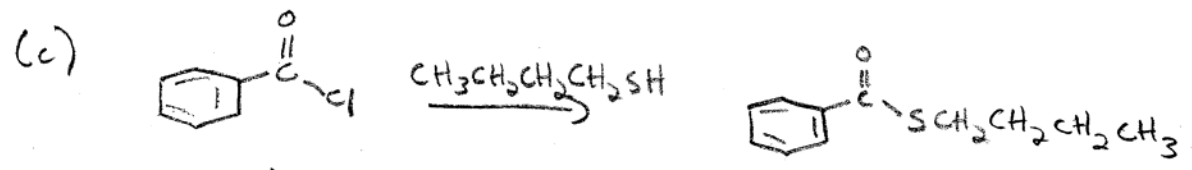
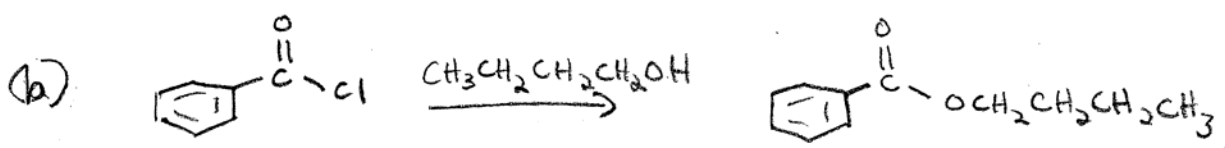
elimination



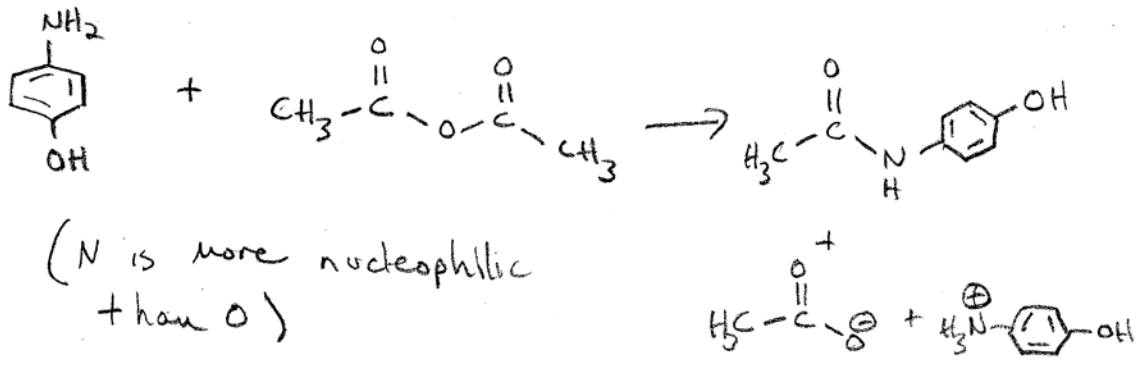
15.19



15.18

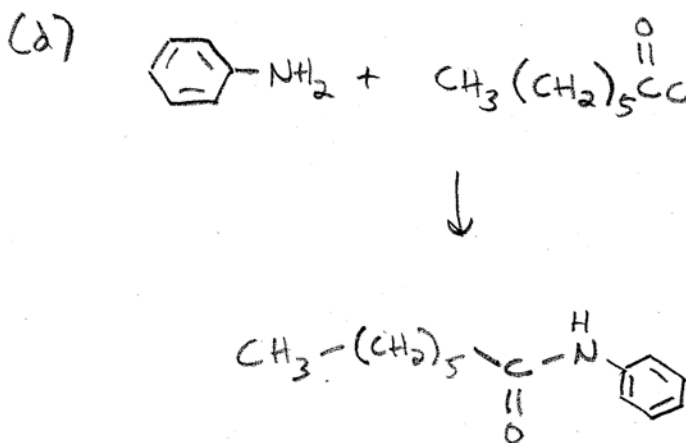
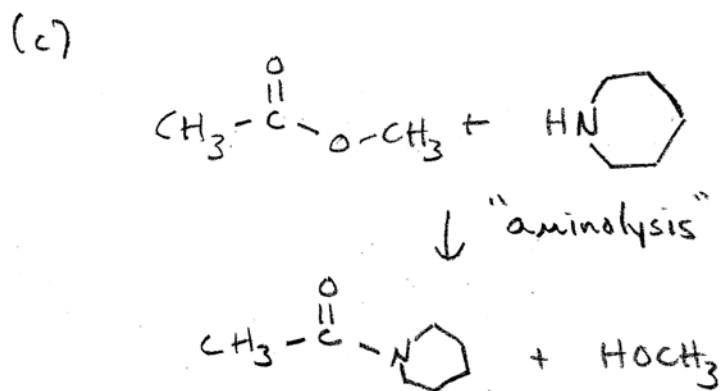
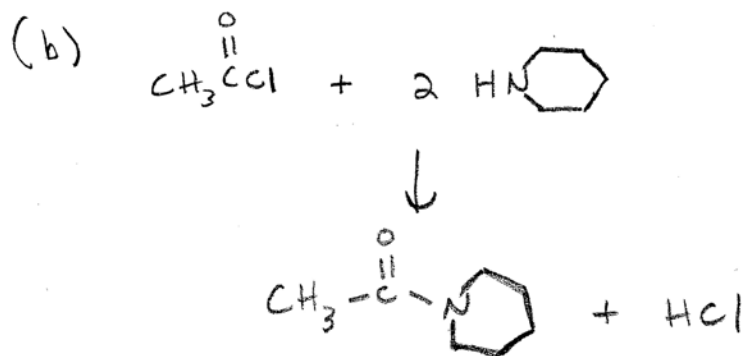
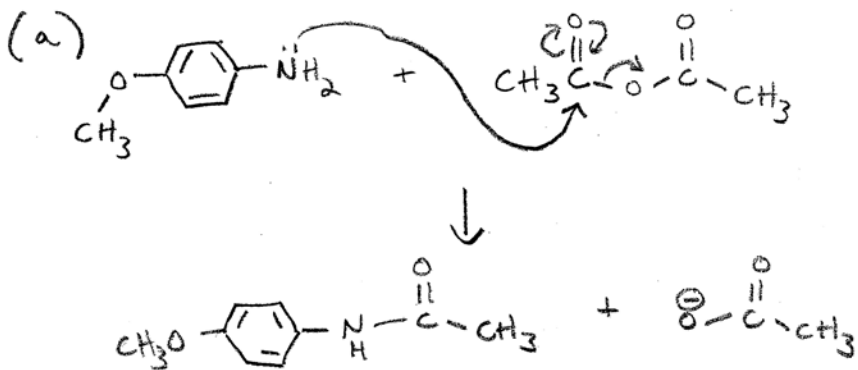


15.22



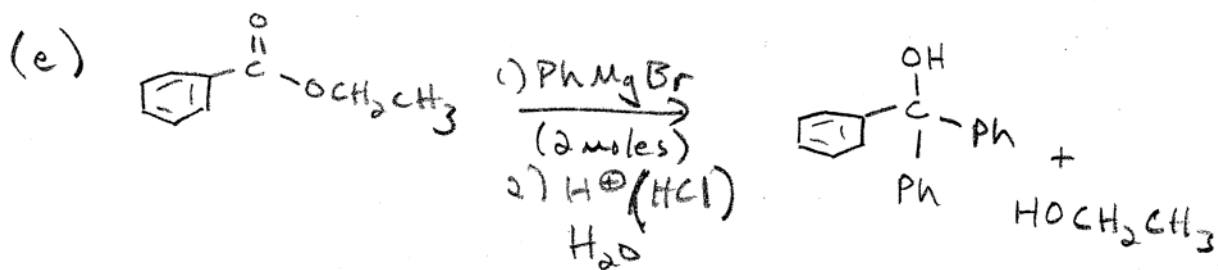
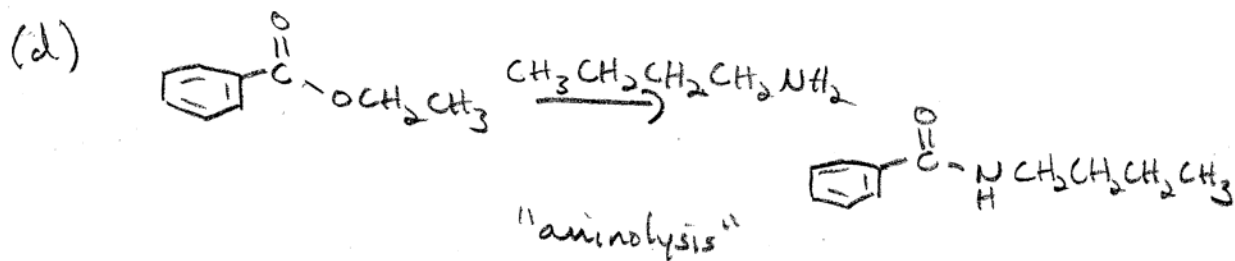
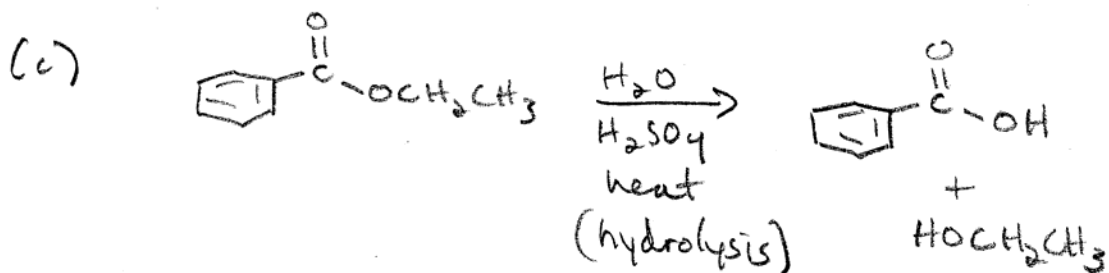
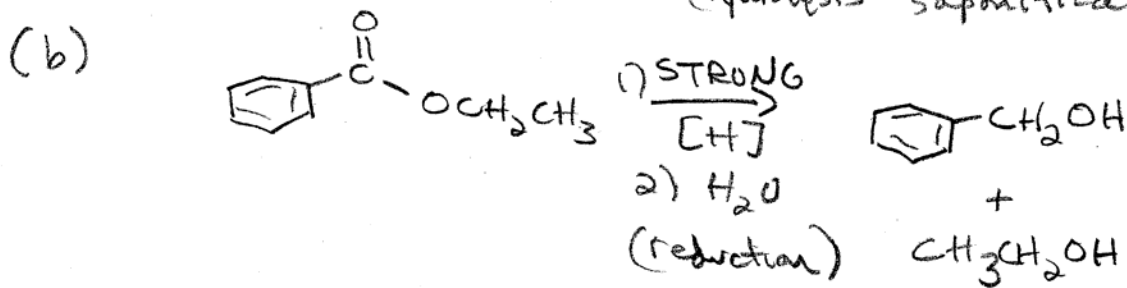
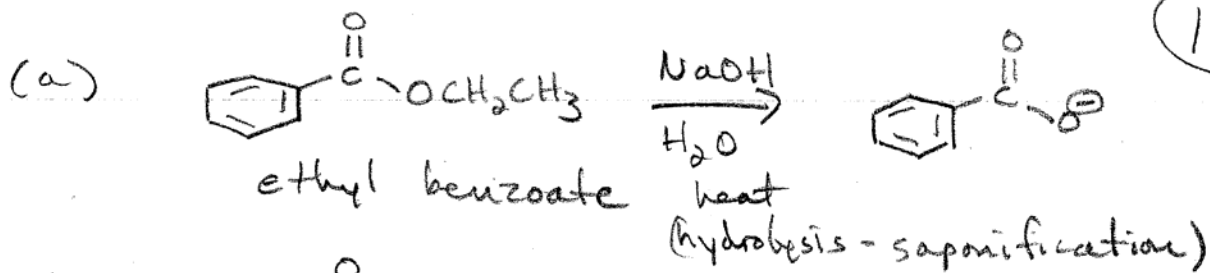
15.24

12

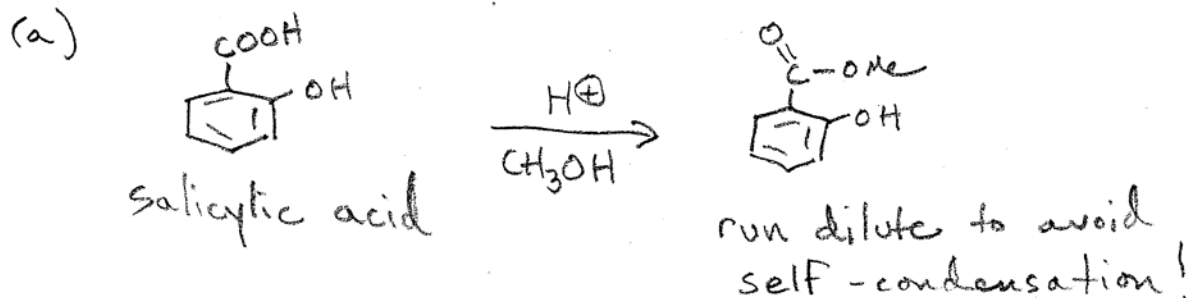


15.25

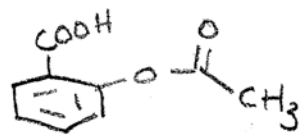
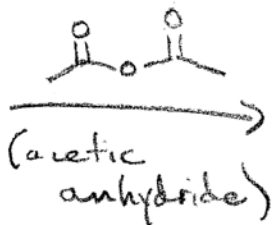
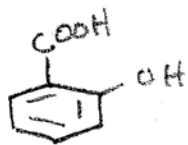
13



15.26



(b)

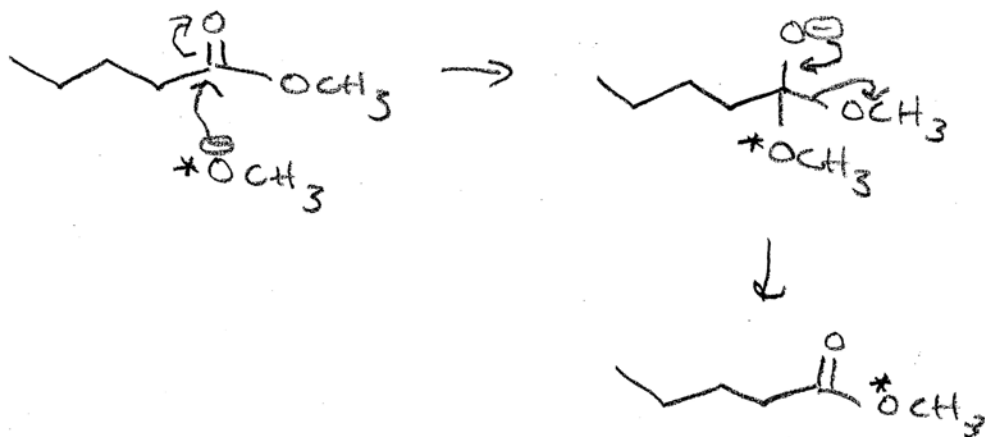


aspirin

(14)

15.45

It may occur:



Label the "starred" oxygen as  $^{18}\text{O}$  and use mass spectrometry to see if any  $^{18}\text{O}$  ("heavy oxygen") is incorporated into the ester.