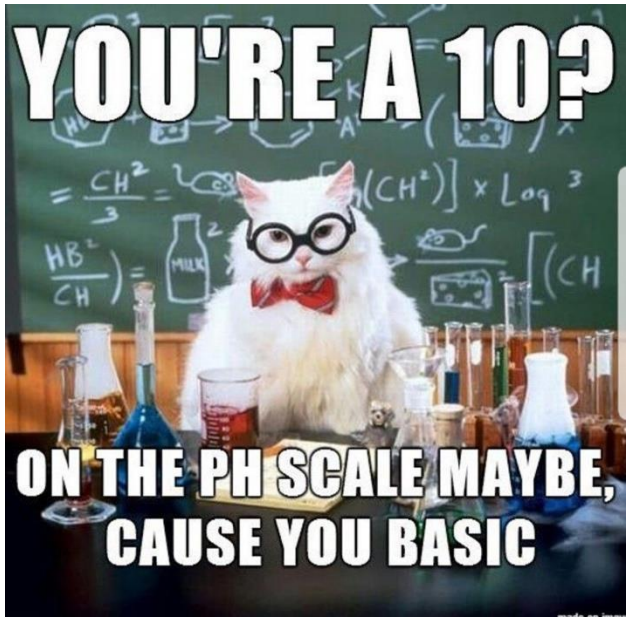
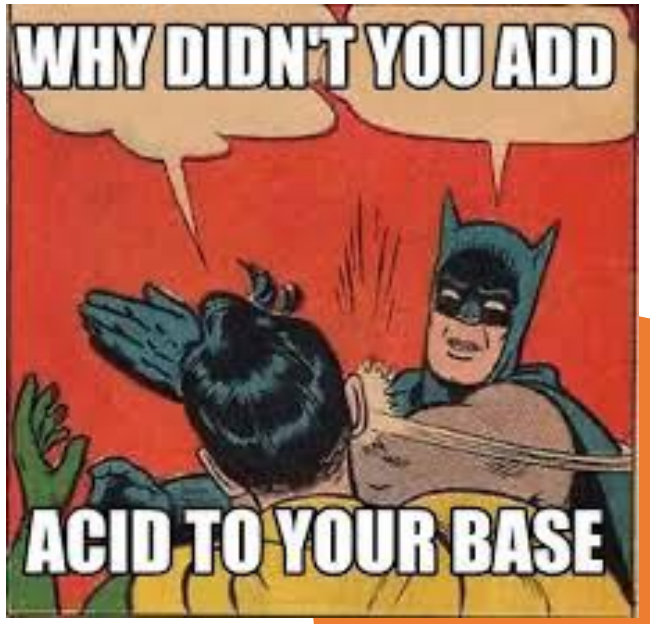
CH. 3 – BASES & ACIDS



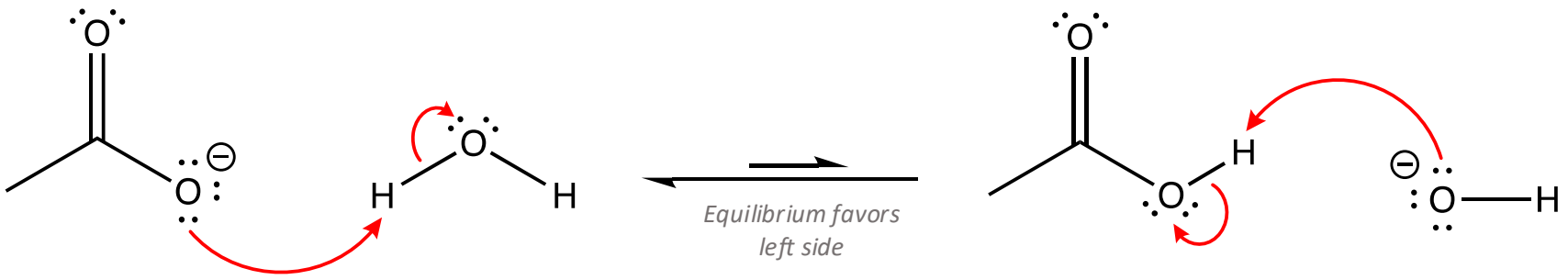




ACID-BASE EQUILIBRIA: Determining the Less Reactive Side

Acid & Base Reactions are generally always in **equilibrium**, and do not often go to completion.

The reaction will always favor the side with less reactive (i.e. weaker) acids and bases.



WEAKER BASE	WEAKER ACID	STRONGER ACID	STRONGER BASE
Resonance stabilized	pK_a = 15.7	pK_a = 4.75	*Localized charge*

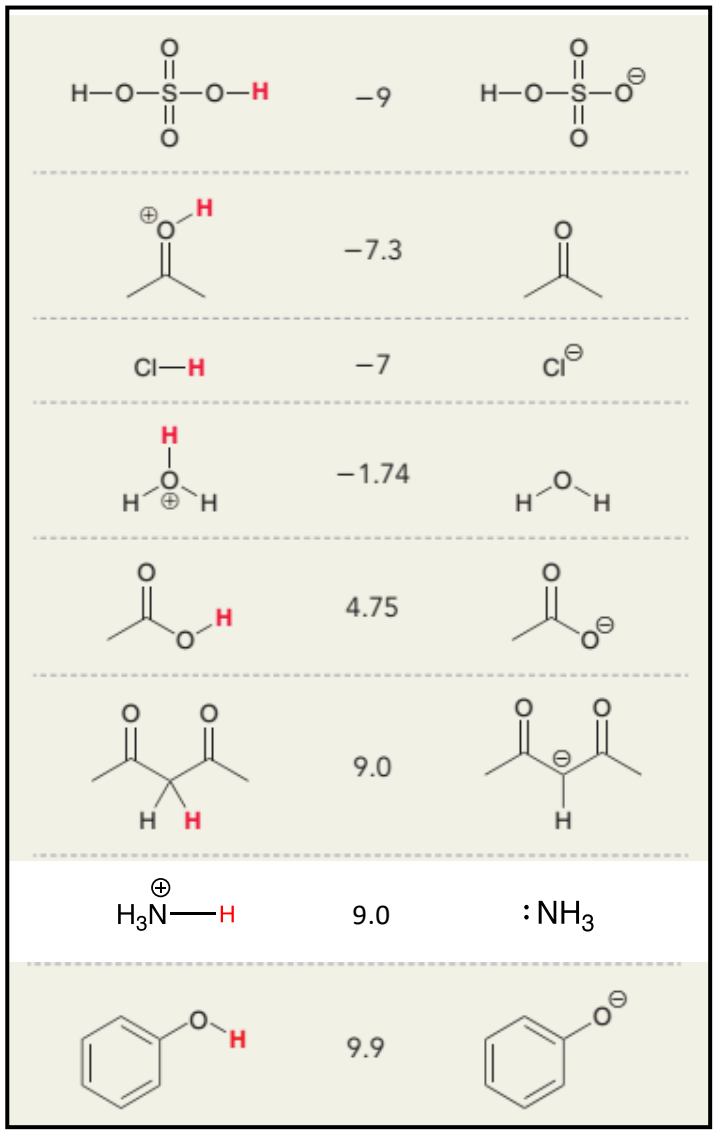
Bases are weaker when the lone pairs (and resultant charge) are stabilized and not willing to pick up a proton (H^+).

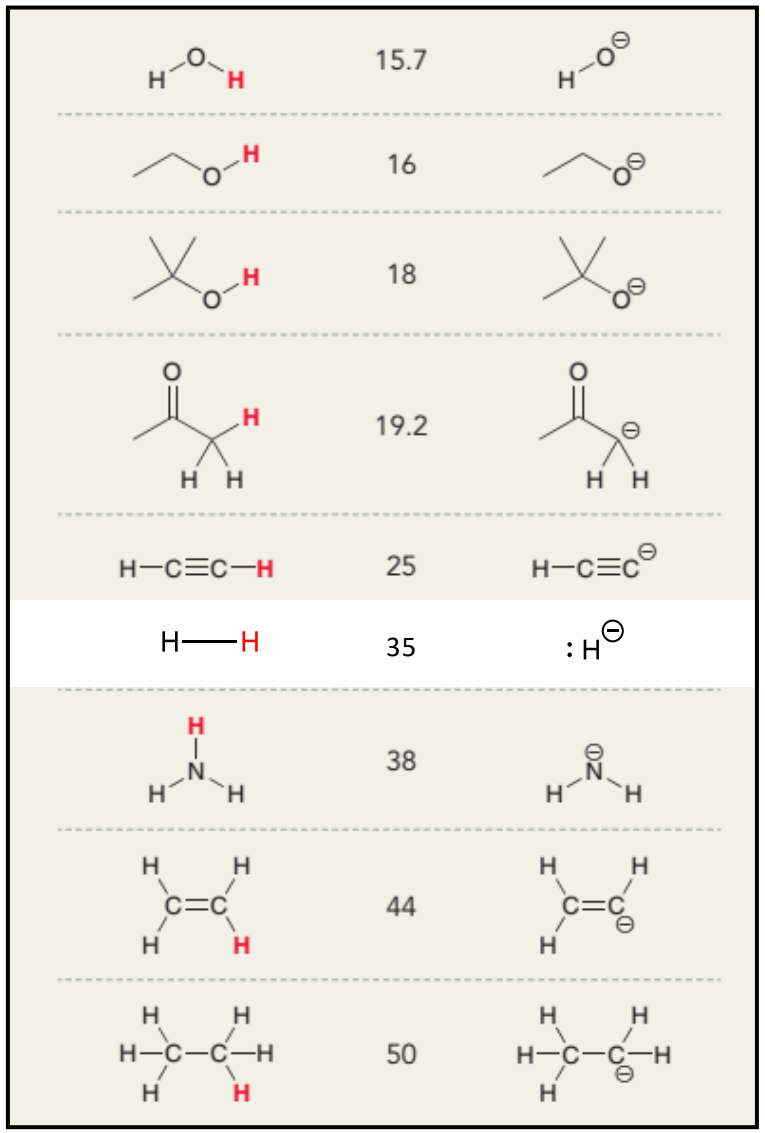
We can use A.R.I.O. to evaluate basicity.

Acids are weaker when they are most stable without losing the proton (i.e. their conjugate bases are reactive and unstable).

We can use pK_a values to evaluate acidity; higher pKa values indicate weaker acids.

QUANTITATIVE PERSPECTIVE: Using pK_a to Evaluate Acidity





You **must memorize** these pK_as. They will likely not be provided on exams or quizzes.

pK_a is used for ACIDS.
pK_b is used for BASES.

When comparing pK_a's, you must compare the compound *before* it loses the proton.

A conjugate base does *not* have the same pK_a as its acid.

Important Note:
This is a useful technique to use when comparing molecules that are significantly different and cannot be evaluated w. ARIO.

QUALITATIVE PERSPECTIVE: Using A.R.I.O. to Evaluate Basicity

Step 1: Draw the conjugate base (CB) of the acid. ARIO is for *bases*.

Step 2: Evaluate the CB using ARIO.

- **A**tom – Which atom is better at holding the (-) charge?
  - Same Row: Which has higher EN?
  - Same Colum: Which has larger atomic radius?
- **R**esonance – Does the (-) charge have resonance?
- **I**nduction – Are adjacent EN atoms withdrawing/donating charge?
  1. Proximity of the EWG/EDG groups
  2. Which atoms are more EN?
- **O**rbital – In what type of orbital are the electrons?
  - Increasing Acidity with more *s* character : $sp^3 < sp^2 < sp$ (e^- closer to nucleus = more acidic)
  - Increasing Basicity with less *s* character : $sp < sp^2 < sp^3$ (e^- farther from nucleus = more basic)

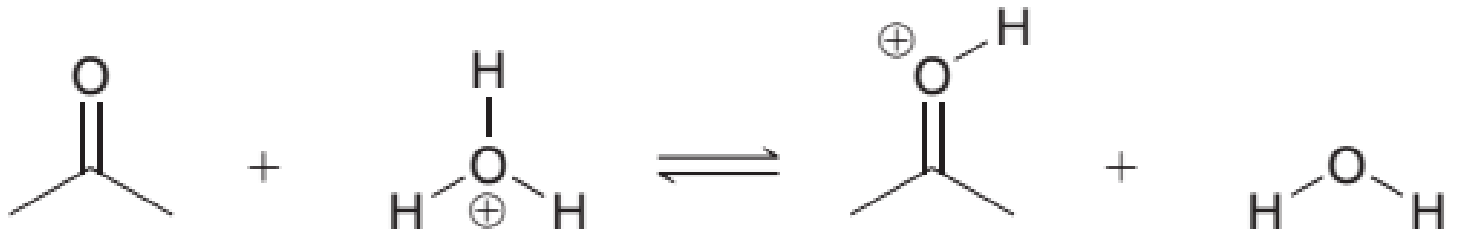
Important Note:
This is a useful technique to use when comparing similar molecules that differ by only 1-2 aspects of ARIO.

Step 3: Consider the resultant acidity. Stronger CB = Weaker Acid.

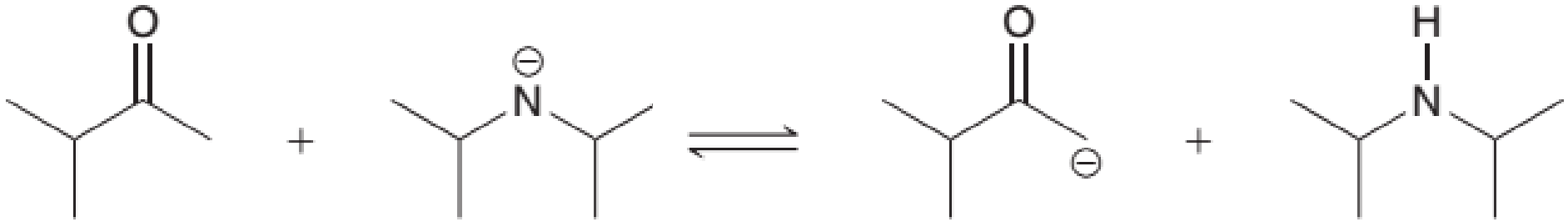
1

Determine which side of the equilibrium the reaction will favor.

a)



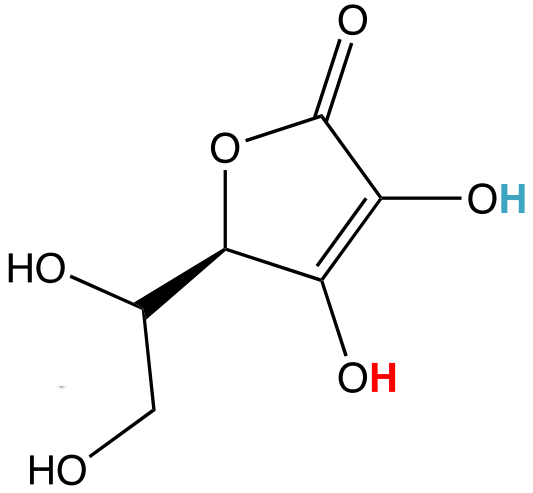
b)



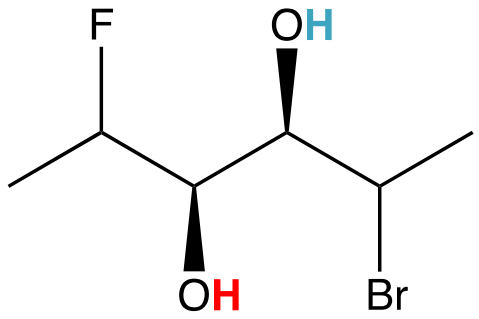
2

Determine which proton is more acidic.

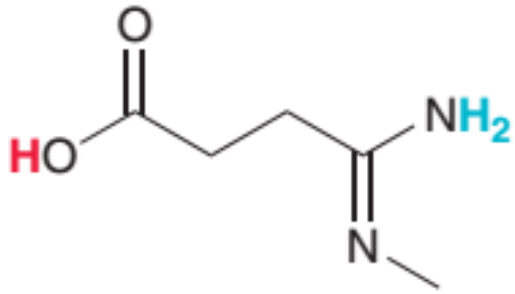
(a)



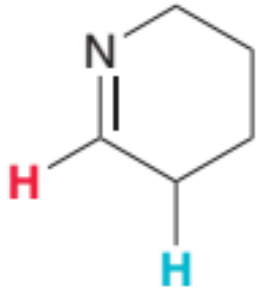
(b)



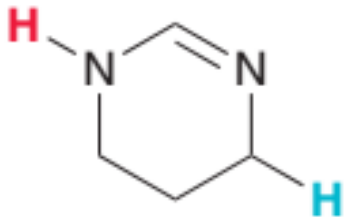
(c)



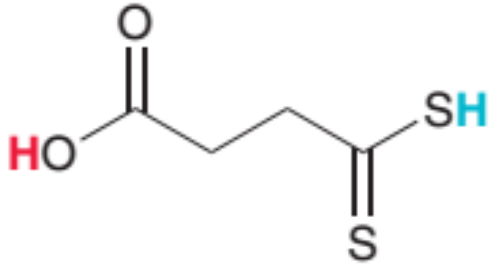
(d)



(e)

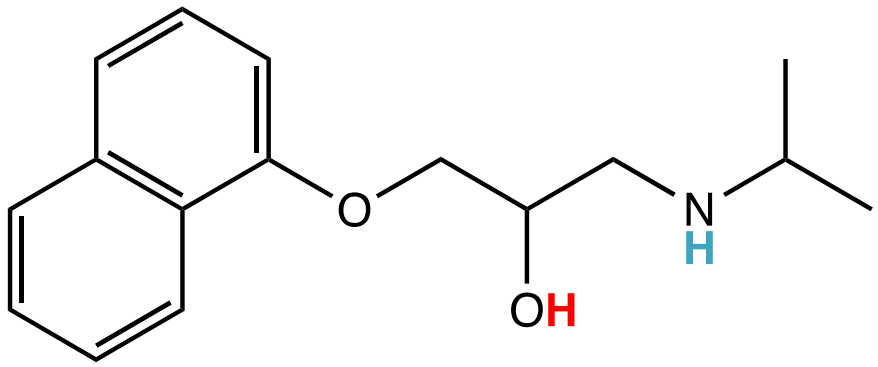


(f)



3

Propanolol is an antihypertensive agent (used to treat high blood pressure). Identify the most acidic proton in the compound, and indicate the approximate expected pK_a:



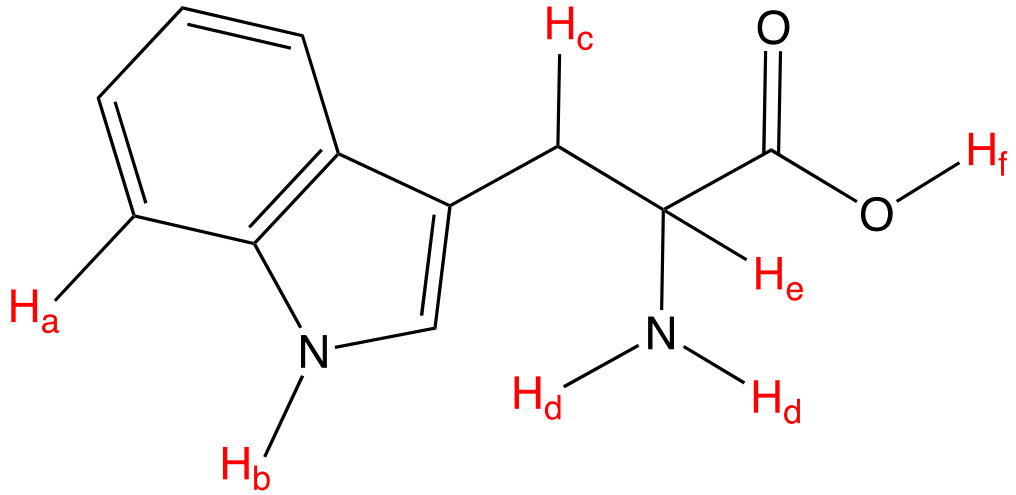
a) The NH proton is most acidic, with pK_a of approx. 38.

b) The NH proton is most acidic, with pK_a of approx. 9.

c) The OH proton is most acidic, with pK_a of approx. 16.

d) The OH proton is most acidic, with pK_a of approx. 10.

Tryptophan, an essential amino acid, is important in the synthesis of the neurotransmitter serotonin in the body. It has the following structure. Circle the **three most acidic protons** in tryptophan.



4

Which base would *not* effectively deprotonate acetylene?

a) *i*-PrMgBr

b) KH

c) $(CH_3O)_2CHCH_2Li$

d) $(i\text{-}Pr)_2NLi$

e) *t*-BuOK

Which base *would* effectively deprotonate benzoic acid?

a) NaCl

b) H_2O

c) NaO_2CCH_3

d) *t*-BuOK

e)

5

Which acid-base would *not* take place as written?

a) $CH_3Li + CH_3CH_2OH \longrightarrow CH_4 + CH_3CH_2OLi$

b) $CH_3C{\equiv}CH + NaOH \longrightarrow CH_3C{\equiv}CNa + H_2O$

c) $HC{\equiv}CNa + H_2O \longrightarrow HC{\equiv}CH + NaOH$

d) $CH_3OH + NaH \longrightarrow CH_3ONa + H_2$

e) $CH_3CO_2H + CH_3ONa \longrightarrow CH_3CO_2Na + CH_3OH$

Which combination of reagents is effective in generating sodium propynide ($CH_3C{\equiv}CNa$)?

a) $CH_3C{\equiv}CH + NaH$

b) $CH_3C{\equiv}CH + (CH_3)_2CHONa$

c) $CH_3C{\equiv}CH + C_2H_5Na$

d) Two of the above

e) All of the above

Ranking Acidity

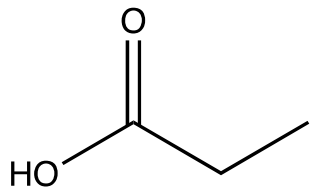
a)

CH_3OH I.

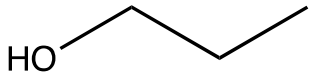
CH_3SH II.

CH_3PH_2 III.

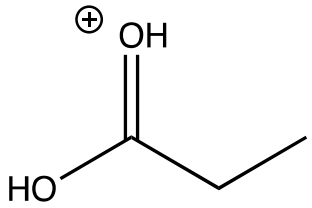
b)



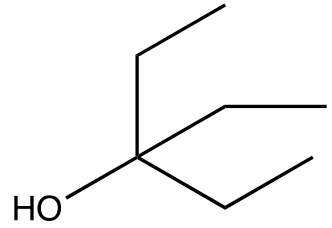
I.



II.

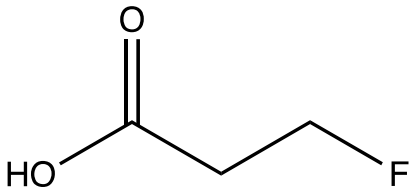


III.

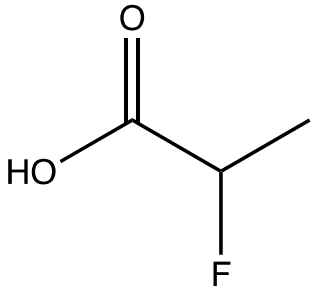


IV.

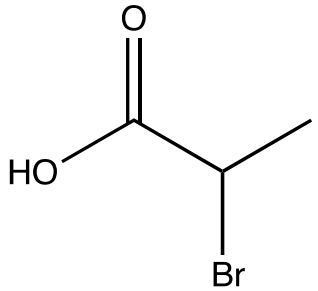
c)



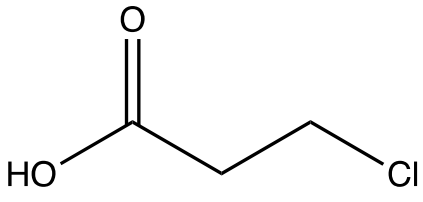
I.



II.



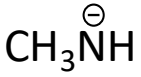
III.



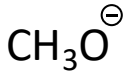
IV.

Ranking Basicity

a)



I.

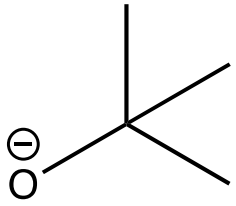


II.

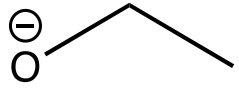


III.

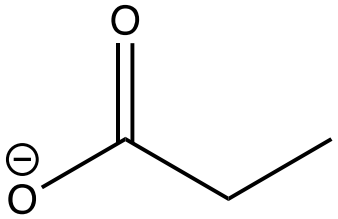
b)



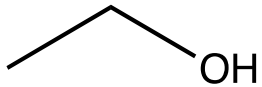
I.



II.

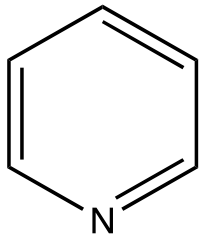


III.

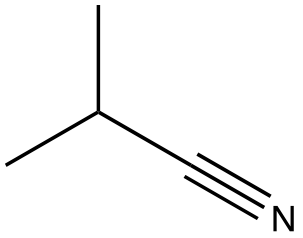


IV.

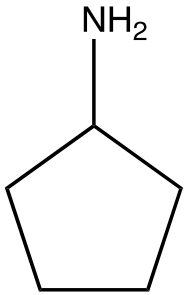
c)



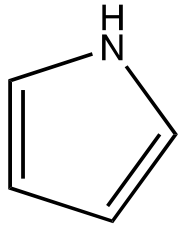
I.



II.



III.



IV.

Leveling Effects: Picking an Appropriate Solvent

Wiley #93. Which of the following solvent *can* be used with $NaNH_2$?

a) CH_3OH

b) H_2O

c) CH_3CH_2OH

d) Liquid NH_3

a) All of these

Wiley #94. Which of the following solvent *cannot* be used with $(CH_3)_3COK$?

a) $(CH_3CH_2)_2O$

b) H_2O

c) $(CH_3)_3COH$

d) Liquid NH_3

e) None of these

Wiley #95. Which of the following solvent *can* be used with $(CH_3)_3CLi$?

a) $CH_3(CH_2)_4CH_3$

b) H_2O

c) CH_3CH_2OH

d) CH_3OH

e) Liquid NH_3

Wiley #96. As a result of the "leveling effect," the strongest acid that can exist in appreciable concentration in aqueous solution is _____.

a) H_2SO_4

b) H_2O

c) HCl

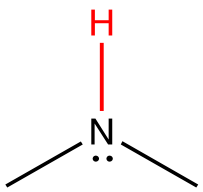
d) HNO_3

e) All of these

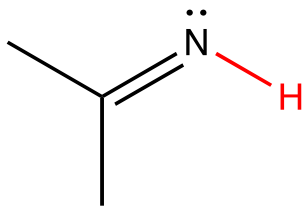
10

Which of the following two molecules is more acidic?

a)

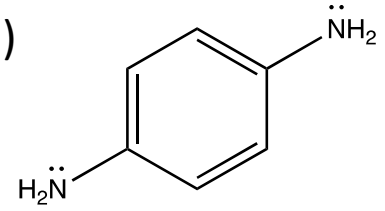


b)

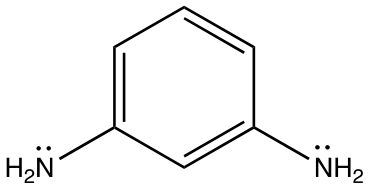


Which of the following two molecules is more basic?

a)



b)

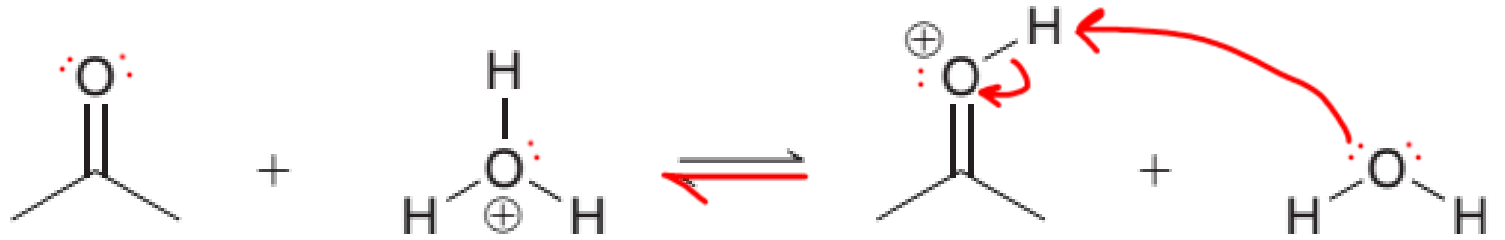


You find a 14M “NH_4OH” solution in your organic chemistry lab. Why is this label misleading?

1 Determine which side of the equilibrium the reaction will favor.

a)

BASE | ACID | Conj. ACID | Conj. BASE



sp^2: 33% *s*
lone pairs *closer to* (+) nucleus
= more stable
= less basic

Weaker Base

$pK_a = -1.7$

Weaker Acid

$pK_a = -7.0$

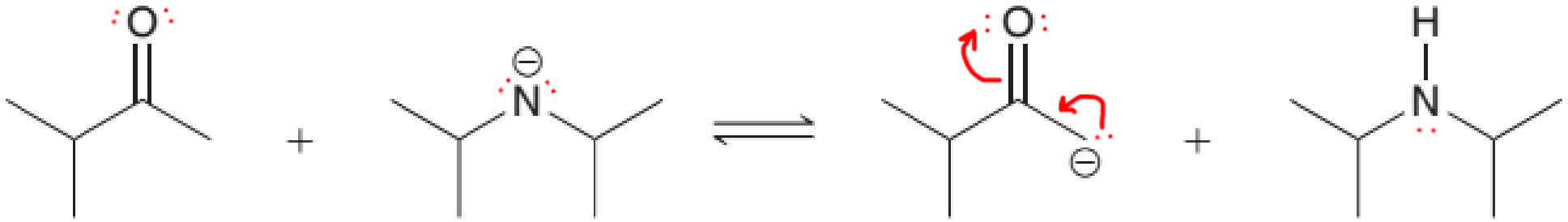
Stronger Acid

Stronger Base

sp^3: 25% *s*
Lone pairs *farther from* (+) nucleus
= less stable
= more basic

b)

ACID | BASE | Conj. BASE | Conj. ACID



$pK_a = 19$

Stronger Acid

Stronger Base

Lone pairs localized on N only.

Weaker Base

Lone pairs delocalized on 2 O atoms. Oxygen is more EN, and the resonance contributes to stability.

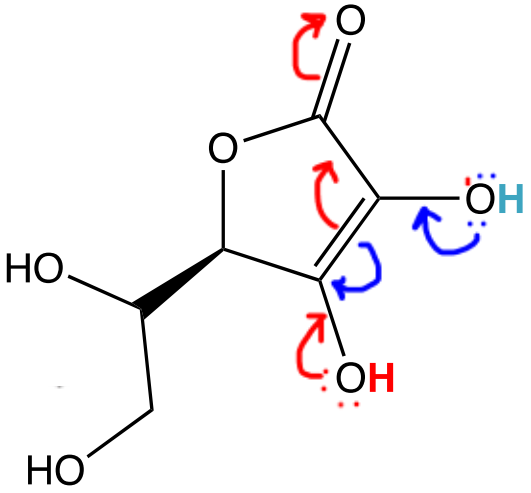
$pK_a = 38$

Weaker Acid

2

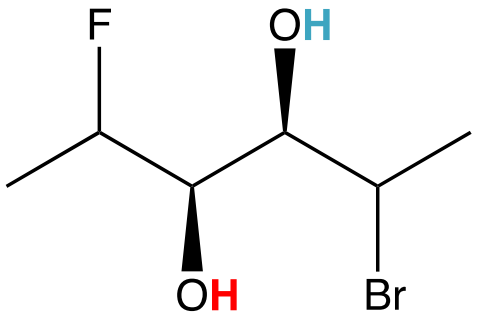
Determine which proton is more acidic.

(a)



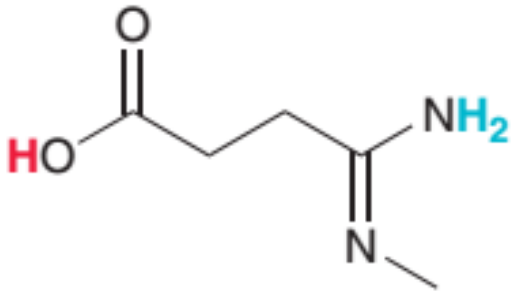
H is more acidic due to greater resonance of conj. base.

(b)



H is more acidic due to greater induction of conj. base due to greater EN_F.

(c)



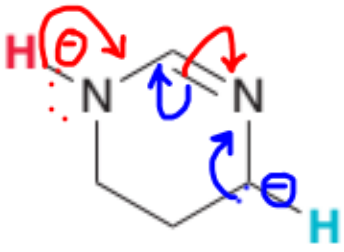
H is more acidic due to conj. base having resonance across two O atoms compared to two N atoms for **H**.

(d)



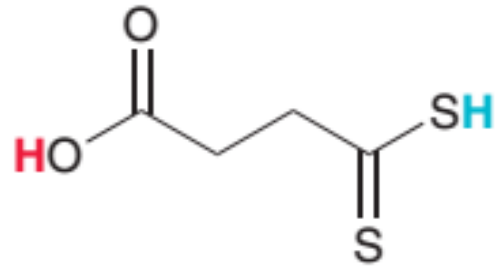
H is more acidic due to greater resonance across C and N in conj. base.

(e)



H is more acidic due to greater resonance of conj. base across two N compared to two C for **H**.

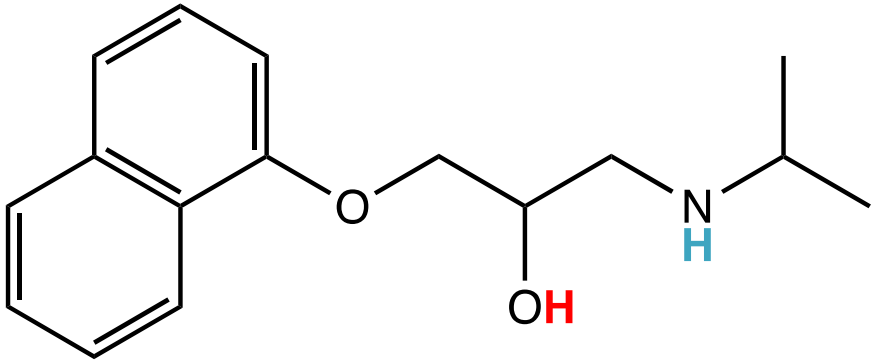
(f)



H is more acidic due to greater resonance of conj. base across two S atoms (larger atomic size than O atom).

3

Propanolol is an antihypertensive agent (used to treat high blood pressure). Identify the most acidic proton in the compound, and indicate the approximate expected pK_a:



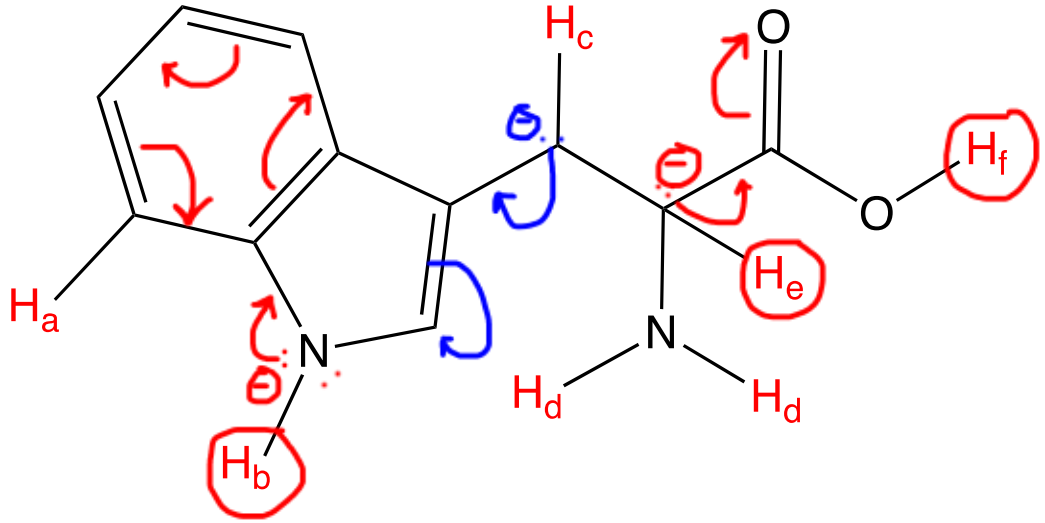
a) The NH proton is most acidic, with pK_a of approx. 38.

b) The NH proton is most acidic, with pK_a of approx. 9.

c) The OH proton is most acidic, with pK_a of approx. 16.

d) The OH proton is most acidic, with pK_a of approx. 10.

Tryptophan, an essential amino acid, is important in the synthesis of the neurotransmitter serotonin in the body. It has the following structure. Circle the **three most acidic protons** in tryptophan.



4

Which base *would not* effectively deprotonate acetylene (HC≡CH, pKa = 25)?

Base	Conj. Acid	pKa
a) *i*-PrMgBr	→ *sp3* C-H	pKa = **50**
b) KH	→ *H2*	pKa = **35**
c) $(CH_3O)_2CHCH_2Li$	→ *same pKa as 'A'*	
d) $(i\text{-Pr})_2NLi$	→ R_2N	pKa = **38**
e) *t*-BuOK	→ tBuOH	pKa = **18**

Which base *would* effectively deprotonate benzoic acid (RCOOH, pKa = 4.75)?

Base	Conj. Acid	pKa
a) NaCl	HCl	pKa = -7
b) H_2O	H3O+	pKa = –1.8
c) CH_3COONa	RCOOH	pKa = 4.75
d) *t*-BuOK	tBuOH	pKa = 18

e) *all of the above*

Which acid-base would *not* take place as written?

a) $CH_3Li + CH_3H_2OH \longrightarrow CH_4 + CH_3CH_2OLi$
pKa = 16 pKa = 50

b) $CH_3C{\equiv}CH + NaOH \longrightarrow CH_3C{\equiv}CNa + H_2O$
pKa = 25 pKa = 15.7

c) $HC{\equiv}CNa + H_2O \longrightarrow HC{\equiv}CH + NaOH$
pKa = 15.7 pKa = 25

d) $CH_3OH + NaH \longrightarrow CH_3ONa + H_2$
pKa = 16 pKa = 35

e) $CH_3CO_2H + CH_3ONa \longrightarrow CH_3CO_2Na + CH_3OH$
pKa = 4.75 pKa = 16

Which combination of reagents is effective in generating sodium propynide ($CH_3C{\equiv}CNa$)?

a) $CH_3C{\equiv}CH + NaH \longrightarrow H_2$
pKa = 25 pKa = 35

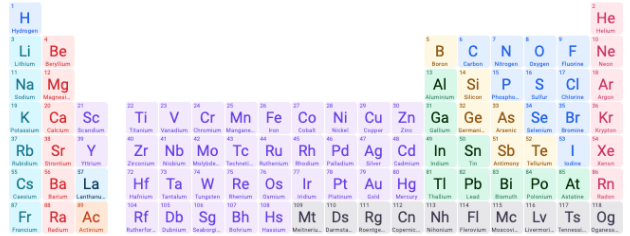
b) $CH_3C{\equiv}CH + (CH_3)_2CHONa \longrightarrow (CH_3)_2CHOH$
pKa = 25 pKa = 18

c) $CH_3C{\equiv}CH + C_2H_5Na \longrightarrow C_2H_6$
pKa = 25 pKa = 50

d) Two of the above

e) All of the above

Ranking Acidity



a) CH_3OH CH_3SH CH_3PH_2

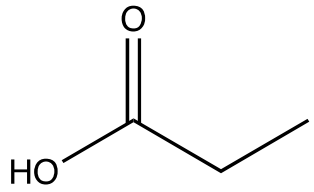
1 > 3 > 2

I. **O has smaller atomic radius than S**
(less volume to diffuse neg. charge of conjugate base e–)

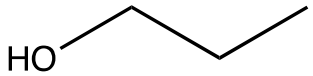
II. **S is more EN than P**
(holds conjug. base e– better than P)

III. **P has bigger atomic radius than O**
(more volume to diffuse CB electrons)
P is less EN than S

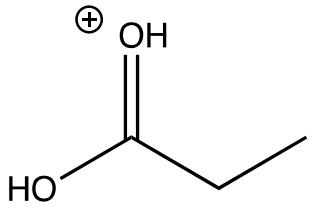
b)



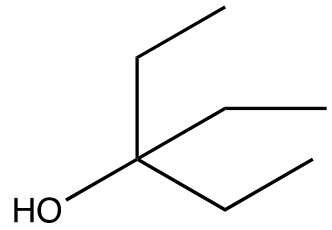
I. **CB** e– in resonance on 2 sp2 oxygens.
pKa = 4.75



II. **CB e–** on 1 sp3 oxygen (no res + 1 R group)
pKa = 16



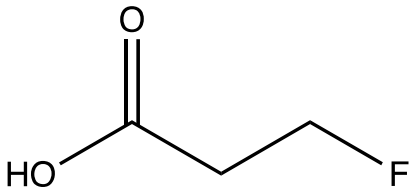
III. **CB e–** on 1 sp2 oxygen (no resonance)
pKa = –7.3 (see chart at start of slides)



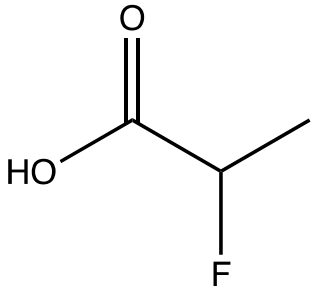
IV. **CB e–** on 1 sp3 oxygen (no res + 3 R groups)
pKa = 18

4 > 2 > 1 > 3

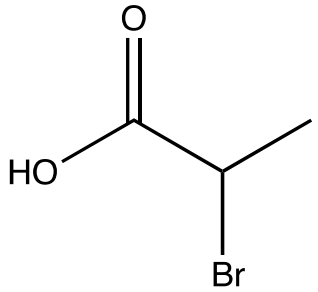
c)



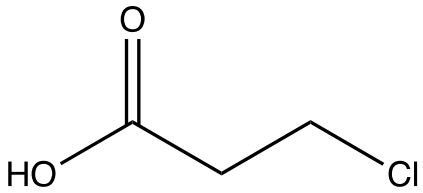
I.



II.



III.



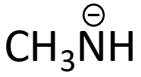
IV.

4 > 1 > 3 > 2

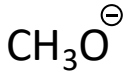
Order of EN determines the **inductive effect** of each halogen: **I > Br > Cl > F**
But, the proximity of the inductor matters more than its identity. Look first at location, then EN value.

Ranking Basicity

a)



I.

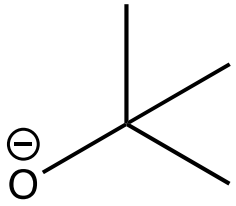


II.

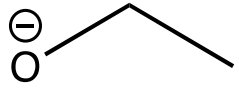


III.

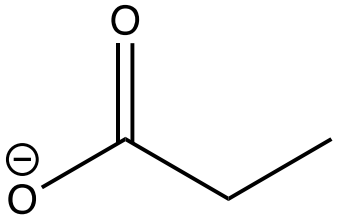
b)



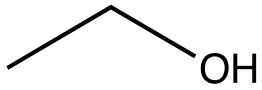
I.



II.

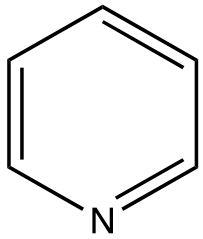


III.

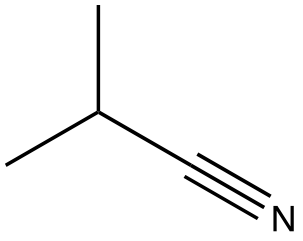


IV.

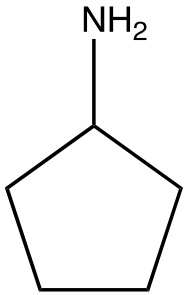
c)



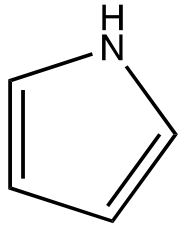
I.



II.



III.



IV.

Leveling Effects: Picking an Appropriate Solvent

Wiley #93. Which of the following solvent *can* be used with $NaNH_2$?

a) CH_3OH

b) H_2O

c) CH_3CH_2OH

d) Liquid NH_3

a) All of these

Wiley #94. Which of the following solvent *cannot* be used with $(CH_3)_3COK$?

(tBuO– is **basic**, w. conj. acid **tBuOH pKa = 18**)

a) $(CH_3CH_2)_2O$ – *no acidic H+ available to interact w. basic reactant*

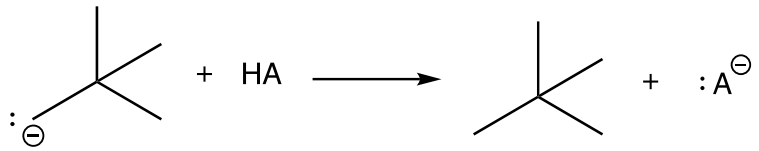
b) H_2O – pKa 15.7 –> *strong enough that it will act as acid w. $tBuO^-$*

c) $(CH_3)_3COH$ – *can always use protonated form of the basic reactant*

d) Liquid NH_3 – pKa 38 –> *not a strong enough acid to act as acid w. $tBuO^-$*

e) None of these

Wiley #95. Which of the following solvent *can* be used with $(CH_3)_3CLi$?



If the solvent has a $pK_a < 50$, then it will act as an acid and not an inert solvent.

a) $CH_3(CH_2)_4CH_3$ (pKa = 50) Only solvent that does not completely neutralize reagent.

b) H_2O (pKa = 15.7)

c) CH_3CH_2OH (pKa = 16)

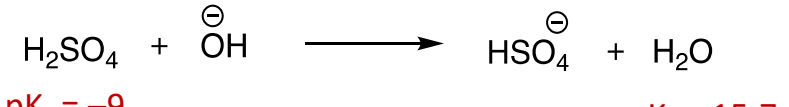
d) CH_3OH (pKa = 16)

e) Liquid NH_3 (pKa = 38)

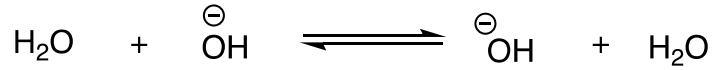
Wiley #96. As a result of the "leveling effect," the strongest acid that can exist in appreciable concentration in aqueous solution is _____.

A.k.a. What acid can exist in equilibrium in water?

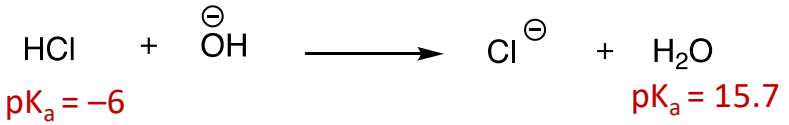
a) H_2SO_4



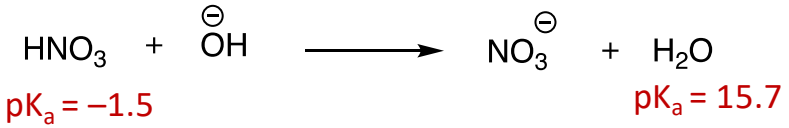
b) H_2O



c) HCl



d) HNO_3



e) All of these