Using Structure to Predict Acidity/Basicity

Strong acid
- relatively unstable acid
- relatively stable conjugate base

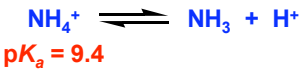
Weak acid
- relatively stable acid
- relatively unstable conjugate base

Strong base
- relatively unstable base
- relatively stable conjugate acid

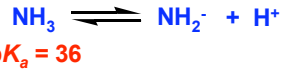
Weak base
- relatively stable base
- relatively unstable conjugate acid

Effect of Structure on pK_a I

1. **Charged vs. noncharged species**
   a charged molecule is more acidic than a neutral molecule



pK_a = 9.4



pK_a = 36

2. **Electronegativity of the atom attached to H**
   the more EN the attached atom, the more acidic the molecule

C < N < O < F
relative electronegativity

$^{-}CH_3 < {}^{-}NH_2 < HO^{-} < F^{-}$
relative stability of conjugate bases

$CH_4 < NH_3 < H_2O < HF$
relative acidity

pK_a = 15.5 pK_a = 40

Effect of Structure on pK_a II

3. Size of attached atom

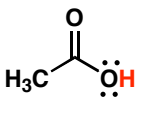
the larger the attached atom, the more acidic (down column)

$I > Br > Cl > F$	$I^- > Br^- > Cl^- > F^-$	$HI > HBr > HCl > HF$
relative size	relative stability of conjugate bases	relative acidity

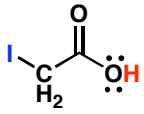
4. Inductive electron withdrawal

a. Magnitude of electronegativity (the more EN, the more acidic)

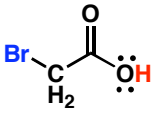
b. Distance away from (-) charged conjugate base (closer = more acidic)



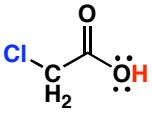
pK_a = 4.76



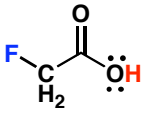
pK_a = 3.15



pK_a = 2.86

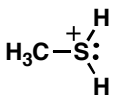


pK_a = 2.81

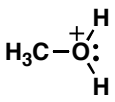


pK_a = 2.66

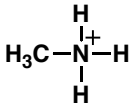
Example: N vs O vs S



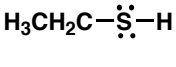
pK_a = -6.8



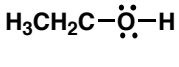
pK_a = -2.4



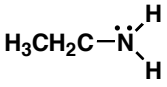
pK_a = 9.8



pK_a = 10.6



pK_a = 15.9



pK_a = 35

Nitrogen is most effective at stabilizing a positive charge and least effective at stabilizing a negative charge

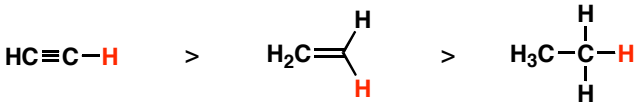
Sulfur is most effective at stabilizing a negative charge and least effective at stabilizing a positive charge

Effect of Structure on pK_a III

5. Hybridization (*sp*, *sp*^{2}, *sp*^{3})

Relative Acidity

sp		*sp*^{2}		*sp*^{3}
50% *s* character	>	33% *s* character	>	25% *s* character



pK_a = 25 pK_a = 44 pK_a = 50

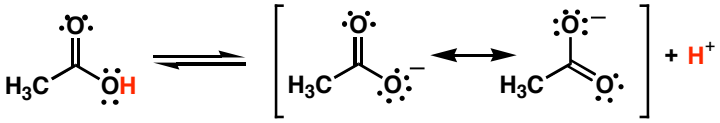
Conjugate base has negative charge, which is stabilized by orbitals with greater *s* character

Effect of Structure on pK_a IV

6. Resonance

resonance stabilizes the negative charge of the conjugate base
the more resonance contributors, the more stable the molecule

pK_a = 15.9



pK_a = 4.76 electron delocalization