



CHEMISTRY 2500

Topic #6: Acids and Bases

Spring 2020

Dr. Susan Findlay



Defining Acidity

- It is common for organic reaction mechanisms to involve one or more elementary steps in which an atom is either protonated or deprotonated to “set up” or to “tidy up” after the main reaction.
- A Brønsted acid is a molecule that loses H^+ to a Brønsted base. The **acidic site** is the hydrogen atom:

- A Brønsted base is a molecule that makes a bond to the hydrogen atom of a Brønsted acid. The **basic site** is the atom/bond donating the electrons used to make this bond:

- Note that the electrons from from the base to the acid.



Quantifying Acidity (pK_a)

- Brønsted acidity is measured using K_a values or pK_a values.
 - K_a is the equilibrium constant for the dissociation of an acid into H^+ and its conjugate base. Where possible, K_a values are measured using water as the solvent.



Strong acids dissociate more easily, giving larger values for K_a .
(more H^+ & A^- = larger numerator; less HA = smaller denominator)

- pK_a is derived from K_a : $pK_a = -\log K_a$

Acids with larger values for K_a (stronger acids) will therefore have low, or even negative, values for pK_a

An acid's strength is determined by the stability of its conjugate base!!!
As the stability of A^- increases, so does the strength of HA .



Quantifying Acidity (pK_a)

- You may recall from CHEM 1000 that I initially introduce pK_a as “the pH at which an acid is exactly half protonated and half deprotonated”.
- In CHEM 2000, you saw the Henderson-Hasselbach equation which demonstrates this relationship mathematically:

$$pH = pK_a + \log \frac{a_{A^-}}{a_{HA}}$$

- This means that we can use pK_a to assess whether or not an acid is likely to remain protonated at a particular pH!
- Biological systems tend to operate at about pH 7. Will a carboxylic acid ($pK_a \approx 5$) be fully protonated in such a system? Will an alcohol ($pK_a \approx 15$) be fully protonated in such a system?



Quantifying Acidity (pK_a)

- The following table, taken from p. 144 of Sorrell, shows typical pK_a values (rounded to the nearest 5) for different types of hydrogen atoms typically found in organic molecules. A similar table can be found on p. 257 of Ogilvie.

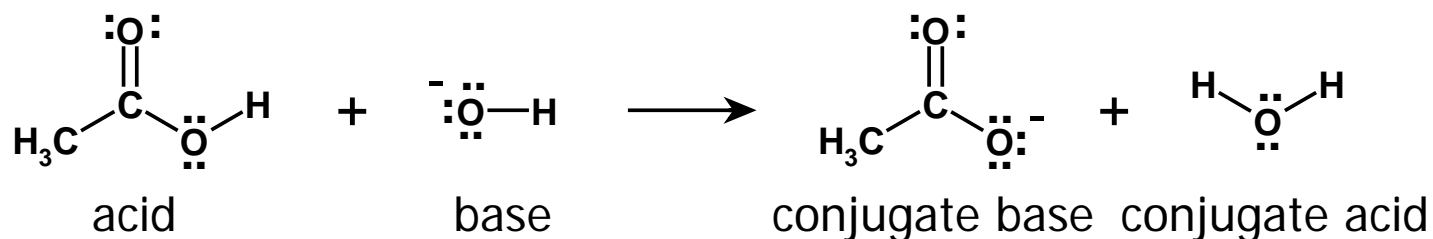
pK_a	Type of Compound
-10	mineral acids: H_2SO_4 , HI, HBr, HCl, sulfonic acids RSO_3H
0	H_3O^+ , H_3PO_4
5	Carboxylic acids, HF, thiophenols $ArSH$, HN_3
10	Weak inorganic acids (H_2S , HCN, NH_4^+), amine salts (RNH_3^+), phenols ($ArOH$), thiols (RSH), aromatic amides ($ArCONH_2$)
15	H_2O , alcohols, thiols (RSH), amides $RCONH_2$
20	ketones (the alpha proton $H-CH_2COR$)
25	Esters (the alpha proton $H-CH_2CO_2R$), alkynes $RCCH$, nitriles ($H-CH_2CN$)
30	Anilines ($ArNH_2$)
40	Ammonia (NH_3), amines (RNH_2), benzylic protons ($ArCH_3$)
45	Arenes (ArH) and alkenes ($RCH=CH_2$)
50	Alkanes

- A more detailed pK_a table can be found in Appendix C of Ogilvie (or on the inside cover of Sorrell).

When is an Acid "Strong Enough"?

- In order for a proton transfer reaction to be product-favoured, it is necessary to use a base whose conjugate acid is weaker than the acid you want to deprotonate. That way, the reactants are the stronger acid and base while the products are the weaker acid and base:

e.g.



- Here, the products are lower in energy than the reactants so the reaction is favoured in the forward direction. Acetic acid ($pK_a = 4.7$) is a stronger acid than water ($pK_a = 14$) therefore acetate is a weaker base than hydroxide.

Strength of a base is **inversely** proportional to the strength of its conjugate acid!



Predicting Acidity

- Why is acetic acid a stronger acid than water? In other words, why is its conjugate base (the acetate anion) more stable than the conjugate base of water (the hydroxide anion)?
- Delocalization of negative charge greatly stabilizes an anion! Draw resonance structures that demonstrate how this applies to this case.



Predicting Acidity

- Phenol is “just an alcohol with a benzene ring”. Why is phenol more acidic than most non-aromatic alcohols?



Predicting Acidity

- Acidity tends to increase left-to-right across a period. Why?

Acid	Conjugate Base	pK _a
H ₃ C-H		48
H ₂ N-H		38
HO-H		14
F-H		3.1

- Acidity tends to increase top-to-bottom down a group. Why?

Acid	Conjugate Base	pK _a
HO-H		14
HS-H		7

Recall that an acid's strength is determined by the stability of its conjugate base...



Predicting Acidity

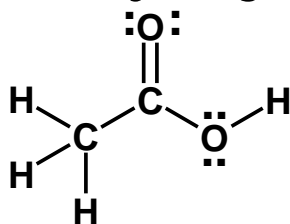
- Terminal alkynes are surprisingly acidic ($pK_a \approx 25$)! Why?
- **Acidity tends to increase with the number of π bonds to the atom you are looking at deprotonating.** This can be viewed as a measure of the s -character of the MO containing the lone pair in the conjugate base – more 's' = lower energy orbital containing electrons = more stable anion.

Acid	Conjugate Base	pK_a
H_3C-H		48
$=CH_2$		44
$\equiv CH$		25
$R-OH_2^+$		~ 0
$R=OH^+$		-4 to -10

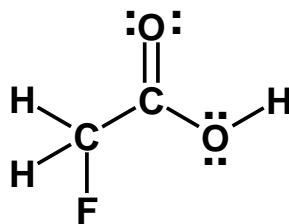
Predicting Acidity

- Another way to increase the strength of an acid is to add electron-withdrawing groups, pulling electron density away from the negatively charged atom in the conjugate base.

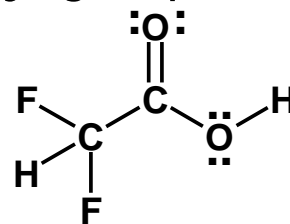
e.g. To increase the acidity of acetic acid, replace one or more hydrogen atoms of the methyl group with fluorine:



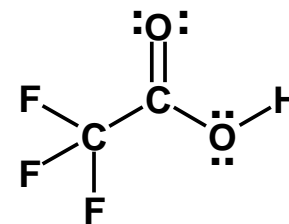
$\text{pK}_a = 4.74$



$\text{pK}_a = 2.66$



$\text{pK}_a = 1.24$



$\text{pK}_a = 0.23$

- This stabilization through σ bonds is called an **inductive effect**.
 - Inductive effects are strongest when the electron-withdrawing groups are close to the acidic hydrogen. *$\text{CF}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$ is not significantly more acidic than $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$.*
- Physical proximity of electronegative atoms can also slightly affect pK_a . This is known as a **field effect**.



Predicting Acidity of Neutral Acids (Summary)

- When you want to compare the strength of two acids, the easiest way is to compare their pK_a values. The acid with the lower pK_a value is stronger.
- When that's not an option, draw the two conjugate bases and look for differences in stability due to:
 - Delocalization of negative charge (resonance!)
 - Electronegativity of atom with negative charge (for atoms in same Period)
 - Size of atom with negative charge (for atoms in same Group)
 - Number of pi bonds to atom with negative charge
 - Inductive effects (EWG within a few sigma bonds of atom with negative charge)
 - Field effects (EWG close in space to atom with negative charge; only look for these if there are no other differences)



Predicting Acidity of Positively Charged Acids

- What if the acid is positively charged? Then its conjugate base won't have a negative charge. You can still compare pK_a values!
- You can also still look for differences in stability due to:
 - Delocalization of positive charge in acid (resonance!) An acid will be less reactive (weaker) if its positive charge is delocalized:
 - Electronegativity of positively charged atom (atoms in same Period). An acid will be less reactive (weaker) if its positive charge is on a less electronegative atom:
 - Size of positively charged atom (atoms in same Group). An acid will be less reactive (weaker) if positive charge is on a larger atom.
 - Inductive effects. (EWG destabilize cations, making them more stronger acids.)



Practice!

- Is hydroxide a strong enough base to deprotonate phenol?
Hint: Start by identifying the most acidic H in phenol.

- Is water a strong enough base to deprotonate methanol?
Hint: Start by identifying the most acidic H in methanol.

Before you use a base in a mechanism, ALWAYS ask yourself "is this base strong enough to deprotonate this acid?"