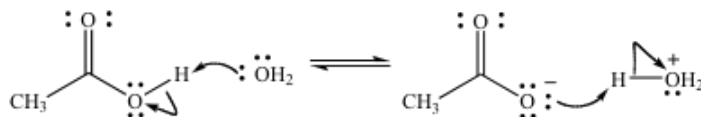
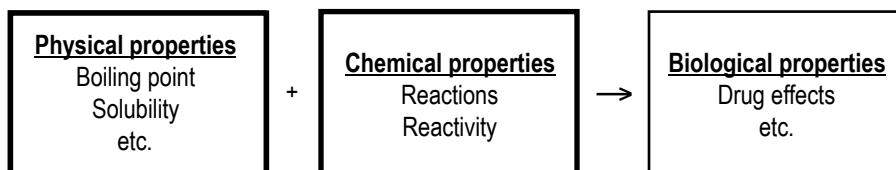


Introduction to Structure and Reactivity: Acids and Bases - Part 1

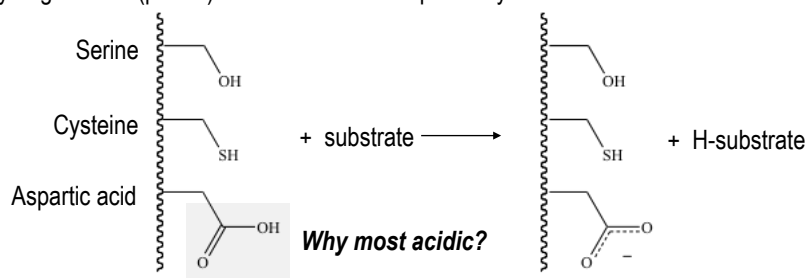


Structure Controls Everything



Example: Enzyme function

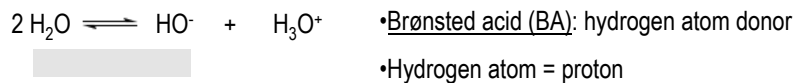
- Hydrogen atom (proton) transfer common step in enzyme reactions



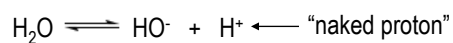
Structure versus Acidity and Basicity

•Suggested reading: OCATSA chapter (email instructor for access)

Begin with a simple example: autoionization of water

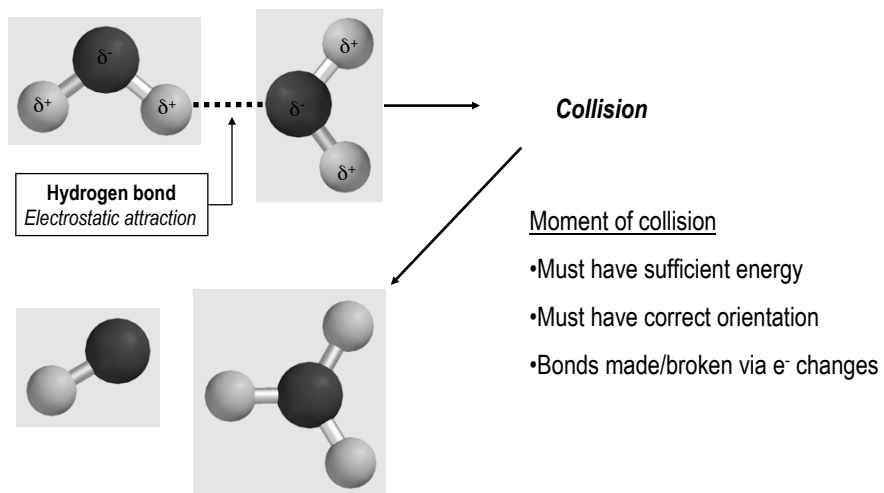
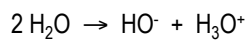


Avoid this common error



Balanced equation does not reveal how or why autoionization occurs.

Autoionization of Water: A Deeper Look

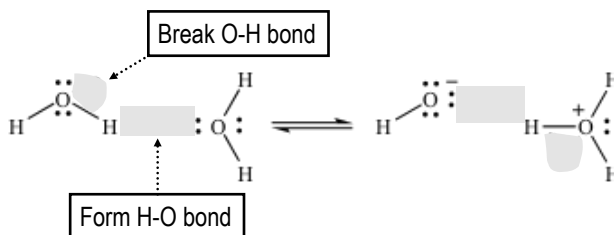


Autoionization of Water: Reaction Mechanism

Reaction mechanism: Step-by-step description of bond changes

• Word description can be lengthy

• Simplify with **curved arrows**



• Reaction mechanism can be single step or many steps

• Useful to explain and predict reaction products

• *Important organic chemistry tool*

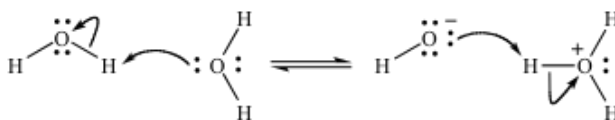
Autoionization of Water: Reaction Mechanism

Nucleophiles and Electrophiles

Many reactions initiated by...

...electrostatics (opposite charges attract)

...electron donor interacting with electron acceptor



Electron acceptor

• Electron poor: +, δ^+ , open octet

• "Electron loving" = **electrophile**

• Lewis acid

• Examples: H_3O^+ , H_3C^+ , $\text{H}_3\overset{\delta^+}{\text{C}}\overset{\delta^-}{\text{Cl}}$

Electron donor

• Electron rich: -, δ^- , lone pairs, pi bonds

• "Nucleus loving" = **nucleophile**

• Lewis base

• Examples: H_2O , HO^- , $\text{H}_2\text{C}=\text{CH}_2$

Autoionization of Water: Reaction Mechanism

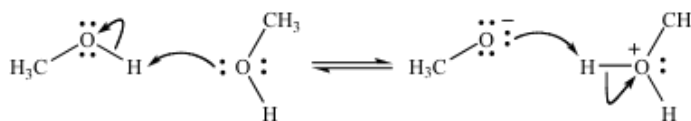
Functional Groups and Mechanisms

Mechanisms are powerful predictive tools

•Example: autoionization of HOH...



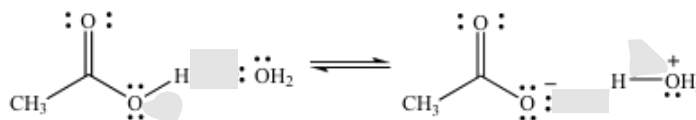
...suggests autoionization of CH₃OH



Proton Transfer Equilibrium Position

How can we determine equilibrium position for proton transfer reaction?

- Quantified by K_{eq} = equilibrium constant
- Example: Ionization of acetic acid (CH₃COOH) in water



$$K_{eq} = \frac{[\text{products}]}{[\text{reactants}]} = \frac{[\text{CH}_3\text{CO}_2^-][\text{H}_3\text{O}^+]}{[\text{CH}_3\text{COOH}][\text{H}_2\text{O}]} \quad [\text{H}_2\text{O}] \sim \text{constant}$$

$$K_a = \frac{[\text{CH}_3\text{CO}_2^-][\text{H}_3\text{O}^+]}{[\text{CH}_3\text{COOH}]} = \frac{[\text{ionization products}]}{[\text{unionized}]} = \text{acid ionization constant}$$

Quantifies extent of acid ionization

K_a and pK_a

	Selected K_a values		pK_a values	
↑ Increasing extent of ionization Increasing acidity	H_2SO_4	$K_a = 1 \times 10^9$	-9	Strong acid
	H_3O^+	$K_a = 6.3 \times 10^1$	-1.8	↓ More extensive pK_a table in handout
	CH_3COOH	$K_a = 1.8 \times 10^{-5}$	4.8	
	NH_4^+	$K_a = 6.3 \times 10^{-10}$	9.2	
	CH_3OH	$K_a = 3.2 \times 10^{-16}$	15.5	
	H_2O	$K_a = 2.0 \times 10^{-16}$	15.7	
	CH_4	$K_a \sim 1 \times 10^{-50}$	~50	Weak acid

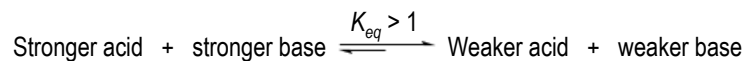
- K_a scale awkward
- Maintain parallel with other thermodynamic conventions
- Define $pK_a = -\log K_a$
 - Lower pK_a = more acidic
 - One pK_a unit = 10x change in acidity

How Does Structure Influence pK_a ?

How can we predict acid/base reaction K_{eq} ?

From general chemistry:

- Equilibrium favors most thermodynamically stable side (lowest G)
- Stability ↑ as acid or base strength ↓
- Therefore equilibrium favors weakest acid/base pair
- ↑ strength of acid (H-B) = ↓ strength of conjugate base (B)
- Therefore need only compare acids or bases (not both)

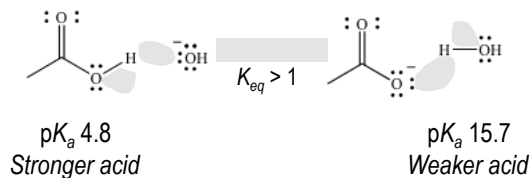


How Does Structure Influence pK_a ?

How do we predict pK_a ?

- How does structure influence acidity and basicity?

Example #1



- Absolute pK_a values difficult to predict
- Why is CH_3COOH stronger acid than H_2O ?
- Why is CH_3CO_2^- weaker base than HO^- ?

How Does Structure Influence pK_a ?

Acid/base reaction = proton tug-of-war

- Base that can share electron pair to make bond to proton keeps proton the most

What influences ability to share electron pair with proton?

- Ability to hold or accommodate the electron pair

↑ **Electron density causes:** ↓ **stability** *Atoms prefer electrical neutrality*
 ↑ **drive to share electron pair**
 ↑ **basicity**

So the real question we need to ask is:

How does structure influence electron density and electron accommodation?

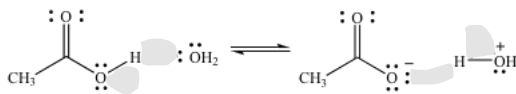
Introduction to Structure and Reactivity: Acids and Bases - Part 2

Lecture Supplement page 204

1	H 1.008 Hydrogen																	He 4.00 Helium																																																																																																																																																																																																																													
2	Li 6.94 Lithium	Be 9.01 Beryllium											B 10.81 Boron	C 12.01 Carbon	N 14.01 Nitrogen	O 16.00 Oxygen	F 19.00 Fluorine	Ne 20.18 Neon																																																																																																																																																																																																																													
3	Na 22.99 Sodium	Mg 24.31 Magnesium	Al 26.98 Aluminum	Si 28.09 Silicon	P 30.97 Phosphorus	S 32.07 Sulfur	Cl 35.45 Chlorine	Ar 39.95 Argon											K 39.10 Potassium	Ca 40.08 Calcium	Sc 44.96 Scandium	Ti 47.88 Titanium	V 50.94 Vanadium	Cr 52.00 Chromium	Mn 54.94 Manganese	Fe 55.85 Iron	Co 58.93 Cobalt	Ni 58.69 Nickel	Cu 63.55 Copper	Zn 65.39 Zinc	Ga 69.72 Gallium	Ge 72.61 Germanium	As 74.92 Arsenic	Se 78.96 Selenium	Br 79.90 Bromine	Kr 83.80 Krypton																																																																																																																																																																																																											
4	Rb 85.47 Rubidium	Sr 87.62 Strontium	Y 88.91 Yttrium	Zr 91.22 Zirconium	Nb 92.91 Niobium	Mo 95.94 Molybdenum	Tc (97.9) Technetium	Ru 101.07 Ruthenium	Rh 102.91 Rhodium	Pd 106.42 Palladium	Ag 107.87 Silver	Cd 112.41 Cadmium	In 114.82 Indium	Sn 118.71 Tin	Sb 121.76 Antimony	Te 127.60 Tellurium	I 126.90 Iodine	Xe 131.29 Xenon																																																																																																																																																																																																																													
5	Cs 132.91 Cesium	Ba 137.33 Barium	La 138.91 Lanthanum	Hf 178.49 Hafnium	Ta 180.95 Tantalum	W 183.85 Tungsten	Re 186.21 Rhenium	Os 190.2 Osmium	Ir 192.22 Iridium	Pt 195.08 Platinum	Au 196.97 Gold	Hg 200.59 Mercury	Tl 204.38 Thallium	Pb 207.2 Lead	Bi 208.98 Bismuth	Po (209) Polonium	At (210) Astatine	Rn (222) Radon																																																																																																																																																																																																																													
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Summary of Part 1

Proton transfer equilibrium:



- **Reaction mechanism:** step-by-step account of bond changes in a reaction
- Illustration of mechanism simplified with **curved arrows**

Nucleophile $\xrightarrow{\quad}$ Electrophile
 Electron source Electron destination

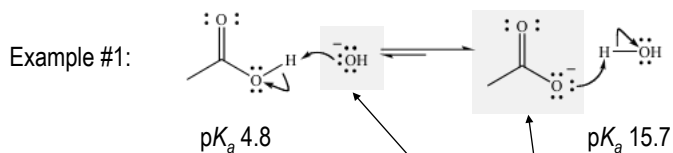
$$K_a = \frac{[\text{CH}_3\text{CO}_2^-][\text{H}_3\text{O}^+]}{[\text{CH}_3\text{COOH}]} = \frac{[\text{ionization products}]}{[\text{unionized}]} = \text{acid ionization constant}$$

Quantifies extent of acid ionization

- $\text{p}K_a = -\log K_a$
- Lower $\text{p}K_a$ = more acidic Examples: H_2SO_4 $\text{p}K_a$ -9; H_2O $\text{p}K_a$ 15.7
- More acidic = more stable conjugate base
- More stable conjugate base = lower electron density; better electron accommodation

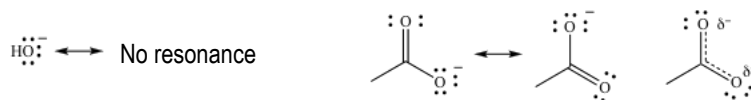
How Does Structure Control Acidity and Basicity?

How does structure influence electron density and electron accommodation?



- Why is CH_3COOH stronger acid than HOH ?
- Why is CH_3CO_2^- weaker base than HO^- ?
- Solution: Examine electron pair accommodation by conjugate bases

How Does Structure Control Acidity and Basicity?



- | | |
|--|--|
| • Electron density not delocalized | • Electron density delocalized by resonance |
| • Higher electron density on oxygen | • Lower electron density on oxygen |
| • Stronger drive to share electron pair | • Weaker drive to share electron pair |
| • Stronger base | • Weaker base |
| • Weaker conjugate acid (H_2O) | • Stronger conjugate acid (CH_3COOH) |
| • H_2O pK_a 15.7 | • CH_3COOH pK_a 4.8 |

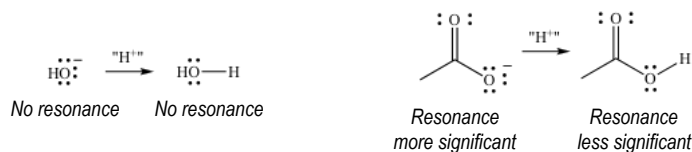
In general...

Resonance usually decreases basicity by removing electron density from the atom(s) that share electron pair with the proton.

How Does Structure Control Acidity and Basicity?

Resonance

- Alternate viewpoint:
- Resonance is a stabilizing feature
 - Process involving loss of resonance is disfavored



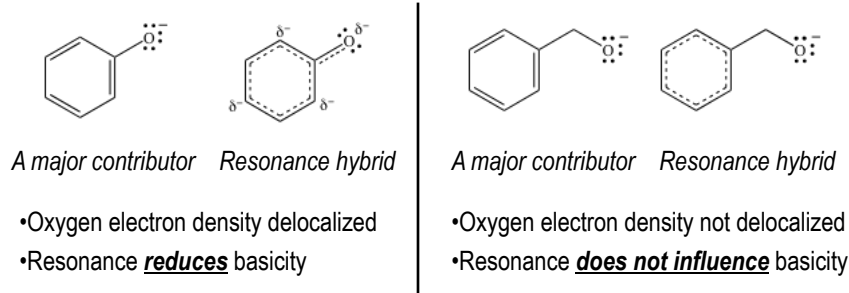
- No loss of resonance upon protonation
- HO⁻ less resistant to protonation
- Stronger base than CH₃CO₂⁻
- Resonance decreased upon protonation
- CH₃CO₂⁻ more resistant to protonation
- Weaker base than HO⁻

How Does Structure Control Acidity and Basicity?

Resonance

Avoid this common misconception: "Resonance always decreases basicity"

- Resonance may decrease basicity (common)
- Resonance may have no impact on basicity (common)
- Resonance may enhance basicity (uncommon)



- Oxygen electron density delocalized
- Resonance **reduces** basicity
- Oxygen electron density not delocalized
- Resonance **does not influence** basicity

The Truth: Resonance usually (but not always) decreases basicity

How Does Structure Control Acidity and Basicity?

Example #2: Rank basicity of these ions: H_3C^- H_2N^- HO^- :F^-

•Resonance influence?

•What is a difference?



Base	CH_3^-	NH_2^-	HO^-	F^-			
EN	C = 2.5	N = 3.0	O = 3.5	F = 4.0			
Predict basicity	CH_3^-	>	NH_2^-	>	HO^-	>	F^-
	<i>Strongest base</i>					<i>Weakest base</i>	
Conjugate acid	CH_4	NH_3	H_2O	HF			
Predict acidity	CH_4	<	NH_3	<	H_2O	<	HF
	<i>Weakest acid</i>					<i>Strongest acid</i>	
pK_a	50	36	15.7	3.2			

In general...

↑ EN of atom that supplies electron pair for bond to proton causes ↓ basicity.

How Does Structure Control Acidity and Basicity?

Example #3: Rank acidity: HF HCl HBr HI

•Convert to conjugate bases; rank basicity

Acid	HF	HCl	HBr	HI			
Conjugate base	F^-	Cl^-	Br^-	I^-			
Resonance	All have same resonance effects						
Electronegativity	F = 4.0	Cl = 3.0	Br = 2.8	I = 2.5			
Predict basicity	F^-	<	Cl^-	<	Br^-	<	I^-
	<i>Weakest base</i>					<i>Strongest base</i>	
Predict acidity	HF	>	HCl	>	HBr	>	HI
	<i>Strongest acid</i>					<i>Weakest acid</i>	
pK_a	3.2	-7	-9	-10			
	<i>Weakest acid</i>					<i>Strongest acid</i>	

The acidity ranking based on electronegativity is wrong!

How Does Structure Control Acidity and Basicity?

Is something besides EN at work?

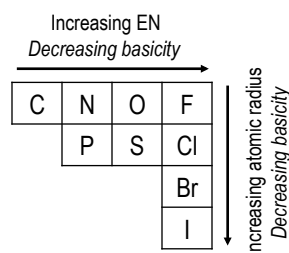
- What else is different among F⁻, Cl⁻, Br⁻, and I⁻?
- A quick check of the periodic table reveals difference in atomic radius
- ↑ atomic radius ↓ electron density (charge per unit volume)
- ↓ electron density ↑ stability and ↓ basicity
- Therefore ↑ atomic radius ↓ basicity

In general...

Larger atomic radius of atom that provides electron pair to proton reduces basicity.

Electronegativity versus atomic radius effects

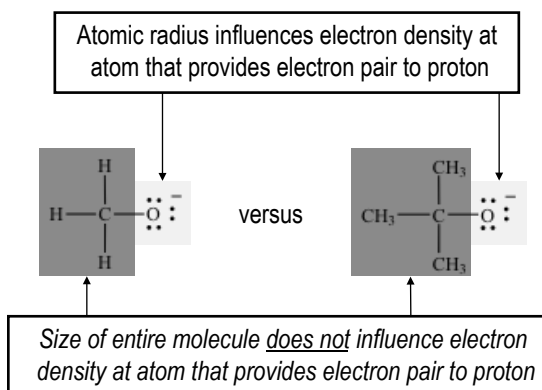
- Which has more influence?



How Does Structure Control Acidity and Basicity?

Atomic Radius Effect

Avoid this common misconception: "Larger bases are weaker bases"

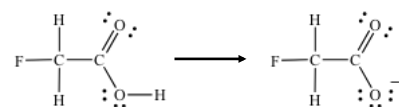


The Truth: Only radius of atom providing electron pair to proton matters

How Does Structure Control Acidity and Basicity?

Example #4: Select the weaker acid

Compare conjugate bases...

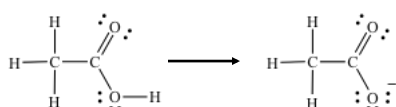


Fluoroacetic acid

Fluoroacetate ion

•Resonance? Same functional group

•Electronegativity? Same functional group



Acetic acid

Acetate ion

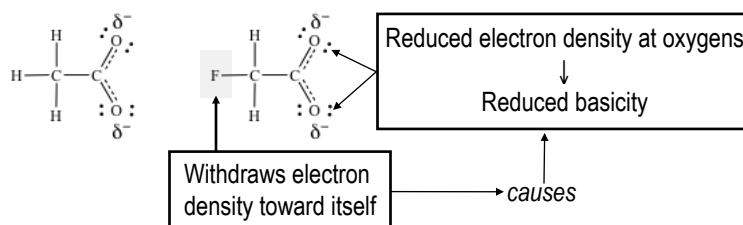
•Atomic radius? Same functional group

How Does Structure Control Acidity and Basicity?

So what is a difference between $\text{FCH}_2\text{CO}_2^-$ and CH_3CO_2^- ?

•F (EN = 4.0) versus H (EN = 2.1)

•Fluorine withdraws electron density from neighboring atoms:



Inductive effect: transfer of charge (electron withdrawal or donation) through a chain of atoms in a molecule by electrostatic induction.

Is our prediction accurate? Predict basicity: $\text{FCH}_2\text{CO}_2^- < \text{CH}_3\text{CO}_2^-$

Therefore predict acidity: $\text{FCH}_2\text{COOH} > \text{CH}_3\text{COOH}$

Test of prediction: FCH_2COOH pK_a 2.1; CH_3COOH pK_a 4.8

How Does Structure Control Acidity and Basicity?

Inductive Effects

Inductive effects depend on electronegativity:

CH_3COOH	ICH_2COOH	BrCH_2COOH	ClCH_2COOH	FCH_2COOH
Acetic acid	Iodoacetic acid	Bromoacetic acid	Chloroacetic acid	Fluoroacetic acid
EN H = 2.1	EN I = 2.5	EN Br = 2.8	EN Cl = 3.0	EN F = 4.0
$\text{p}K_a$ 4.8	$\text{p}K_a$ 3.2	$\text{p}K_a$ 2.9	$\text{p}K_a$ 2.8	$\text{p}K_a$ 2.1

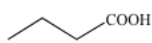
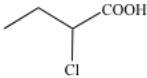
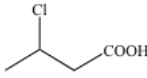
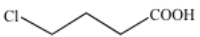
Inductive effects depend on number of electron-withdrawing or electron-donating groups:

CH_3COOH	ClCH_2COOH	Cl_2CHCOOH	Cl_3CCOOH
Acetic acid	Chloroacetic acid	Dichloroacetic acid	Trichloroacetic acid
$\text{p}K_a$ 4.8	$\text{p}K_a$ 2.8	$\text{p}K_a$ 1.3	$\text{p}K_a$ 0.64

How Does Structure Control Acidity and Basicity?

Inductive Effects

Inductive effects depend on distance:

			
Butyric acid $\text{p}K_a$ 4.82	2-Chlorobutyric acid $\text{p}K_a$ 2.86	3-Chlorobutyric acid $\text{p}K_a$ 4.05	4-Chlorobutyric acid $\text{p}K_a$ 4.52

How Does Structure Control Acidity and Basicity?

Formal Charge

Example #5: How does formal charge influence basicity?

- Negative formal charge = excess electron density
 - = greater drive to share electron density
 - = enhances basicity

HO⁻

versus

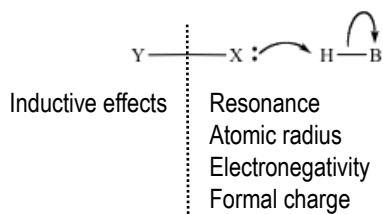
HOH

- Negative formal charge on oxygen
- Stronger base than HOH

- No formal charge on oxygen
- Weaker base than HO⁻

How Does Structure Control Acidity and Basicity?

Which effects do I consider?



Relative strength of structural effects?

Resonance > atomic radius > electronegativity > inductive effects

Formal charge?

- Exceptions exist
- Sequence applies to other types of reactivity as well (ionic substitution reactions, etc.)