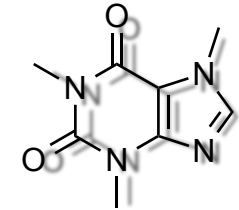


Chem 2500

Chapter 6

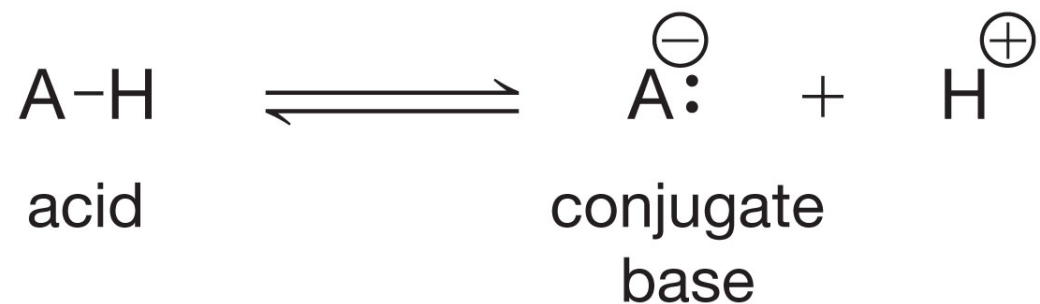
Acids and Bases

(sections 6.1-6.9)



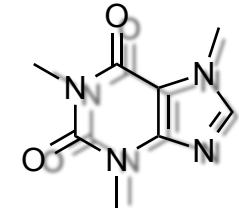
Brønsted Acid-Base Reactions

- ***Brønsted Acid*** – Proton (H^+) donor
- ***Brønsted Base*** – Proton (H^+) acceptor
- Generic equilibrium dissociation of an acid:



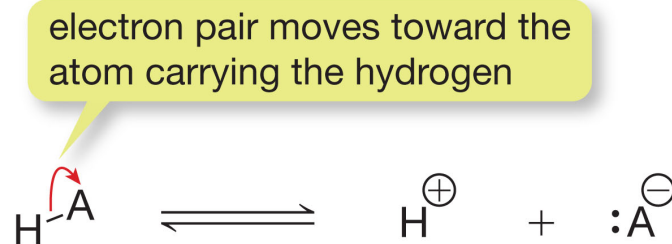
- It is important to remember that H^+ does not exist by itself. H^+ (acids) ‘ride’ on other, carrier molecules, bases.

Brønsted Acid-Base Reactions

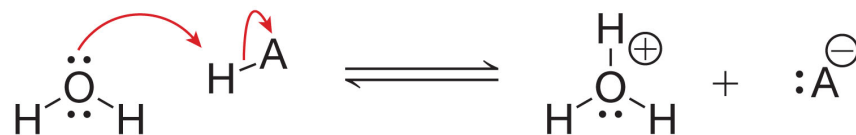


- In acid-base reactions, it is important to always show the carrier base molecule:

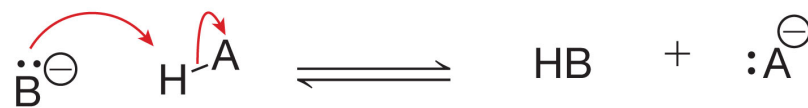
Simplified dissociation of an acid



What happens in water

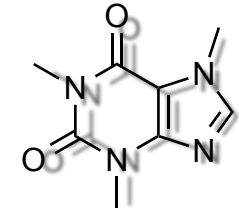


What happens in organic solvents

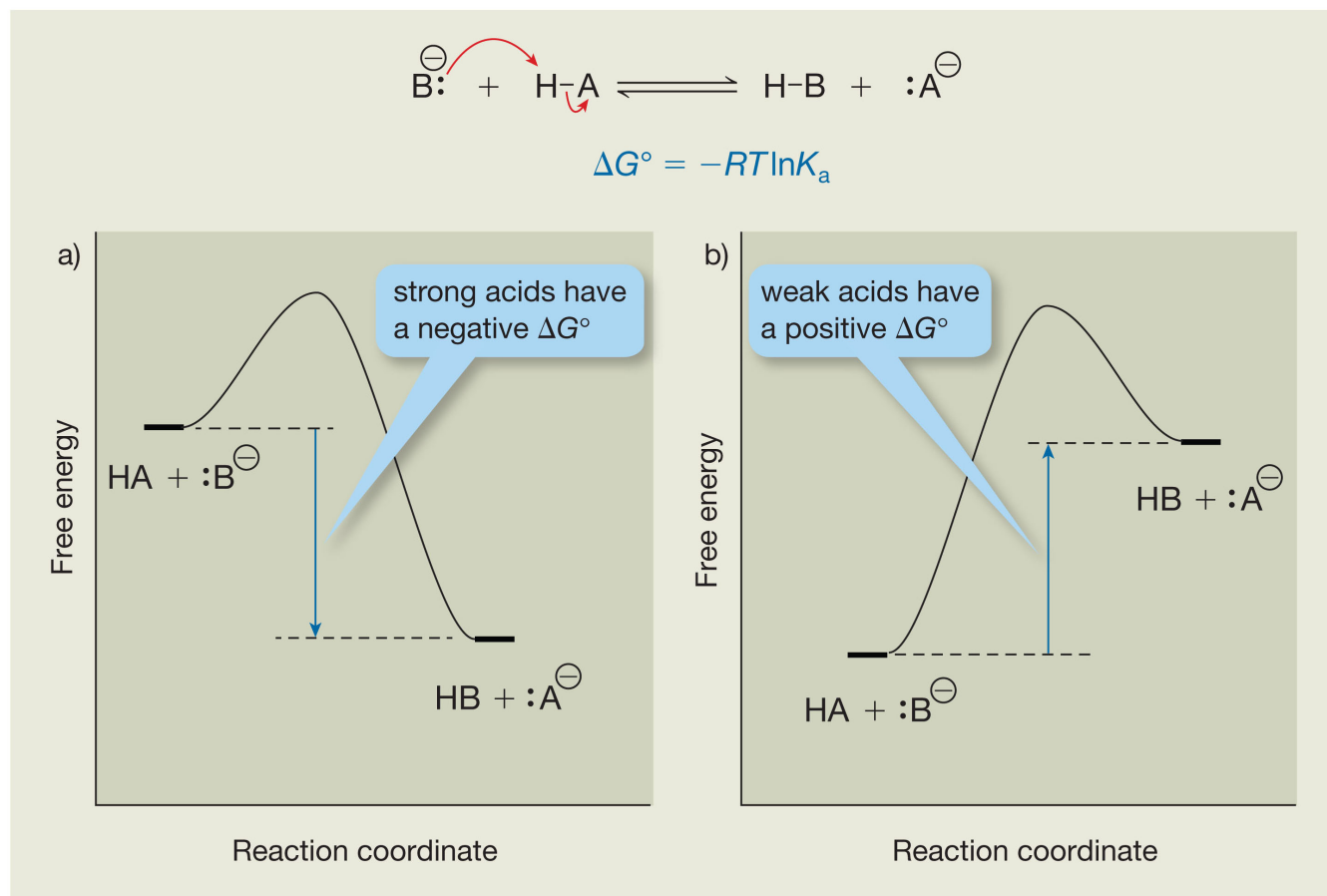


generalized base

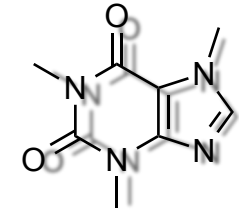
Free Energy and Acid Strength



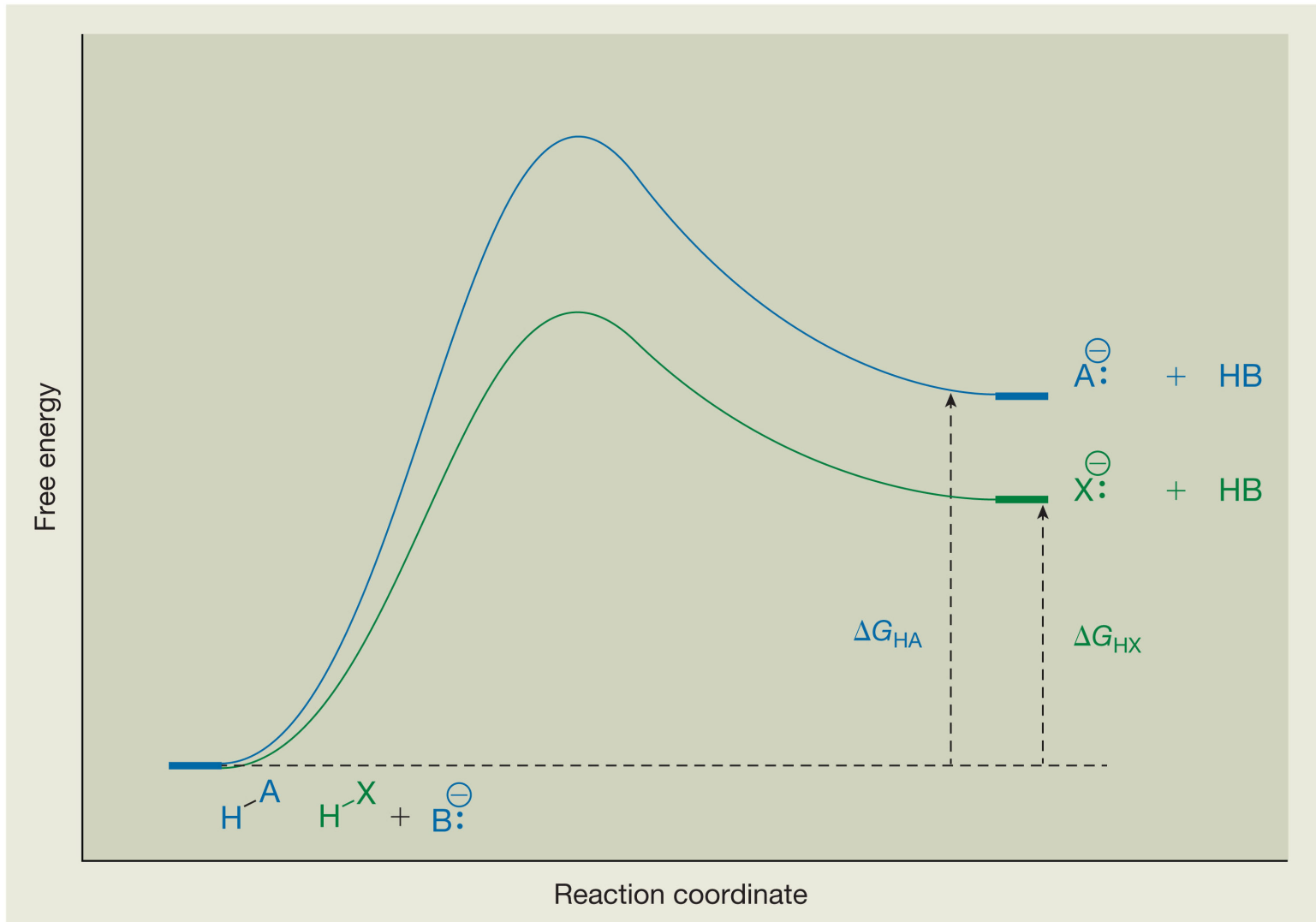
- Strong acids dissociate much more readily than weak acids.
- The strength of an acid can be described by its pK_a value.



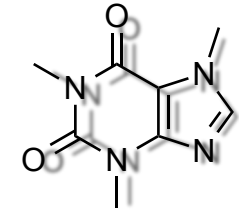
Free Energy and Acid Strength



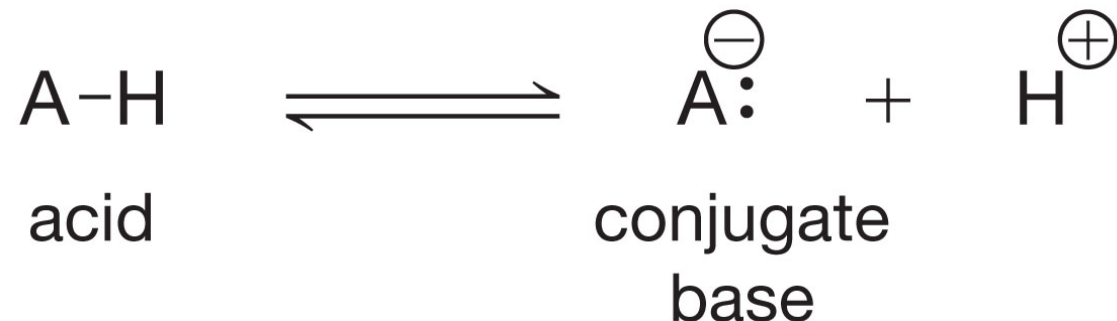
- Assessing relative strengths of different acid/bases is crucial to understanding reaction mechanisms.
- There are both quantitative and qualitative methods of determining the strength of acids and bases.



Qualitative Estimates of Relative Acidities

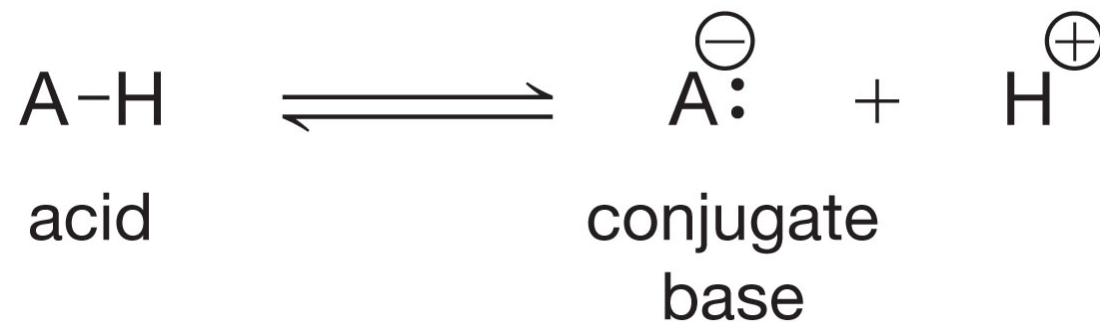
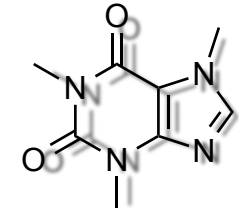


- Many organic acids are neutral and so their conjugate bases are (-) charged:



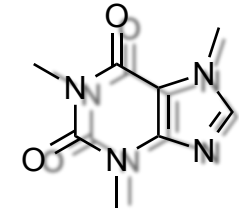
- It may seem counterintuitive, but we can determine relative acidities by looking at the relative stabilities of the conjugate bases.
- The strength of a base is related to its ability to accommodate negative charge:
 - Bases that stabilize negative charges readily are weak (lower ΔG°)
 - Bases that do not stabilize negative charges are much stronger (higher ΔG°).

Qualitative Estimates of Relative Acidities



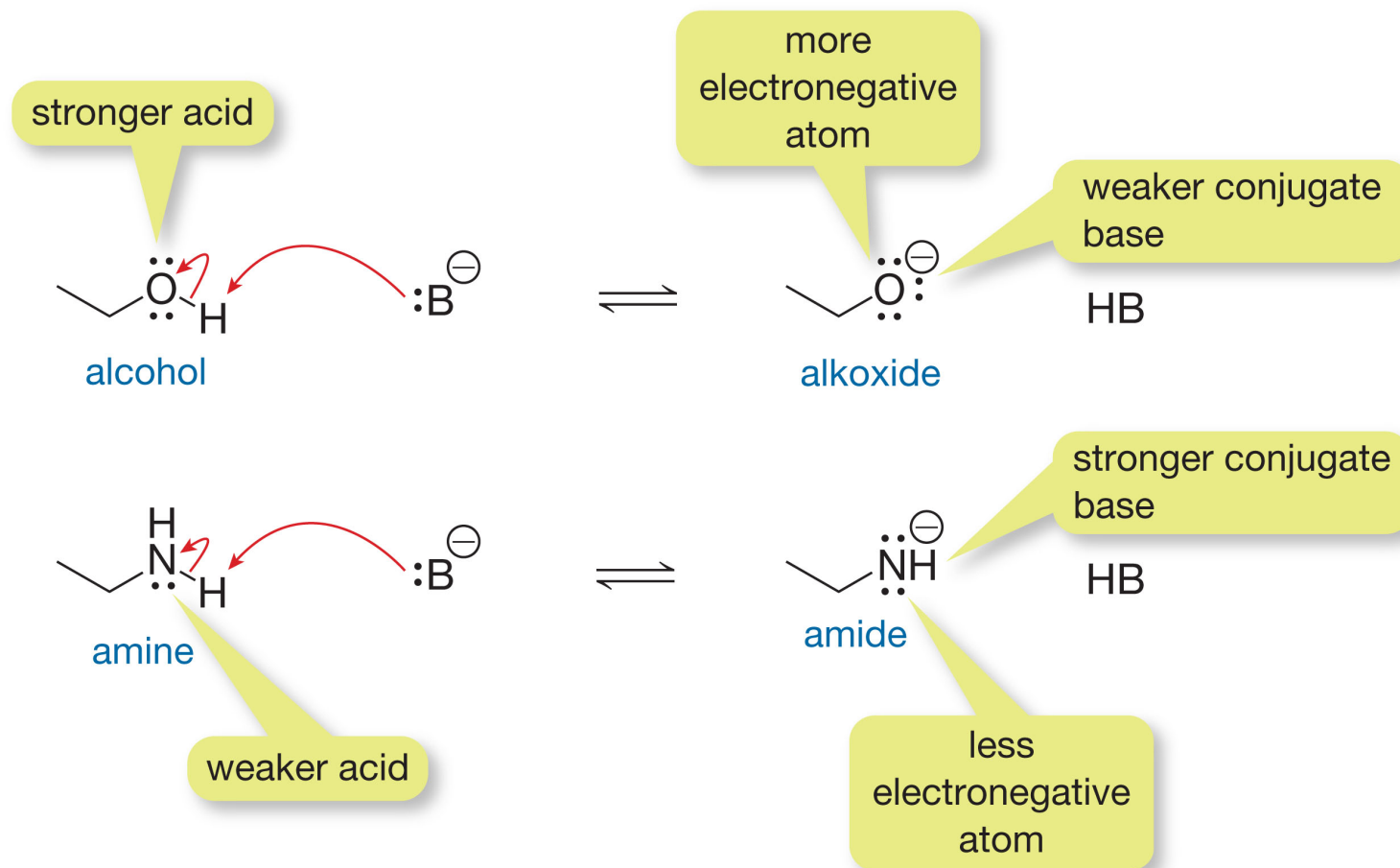
- The relative ability of a base to stabilize negative charge can be estimated using one of five factors:
 1. Electronegativity
 2. Atomic Size
 3. Induction
 4. Hybridization
 5. Charge Delocalization

Qualitative Estimates of Relative Acidities

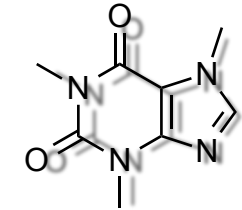


1. Electronegativity

- The electronegativity of the atom carrying the negative charge has a large impact on base stability – a negative charge on a more electronegative atom is more stable:

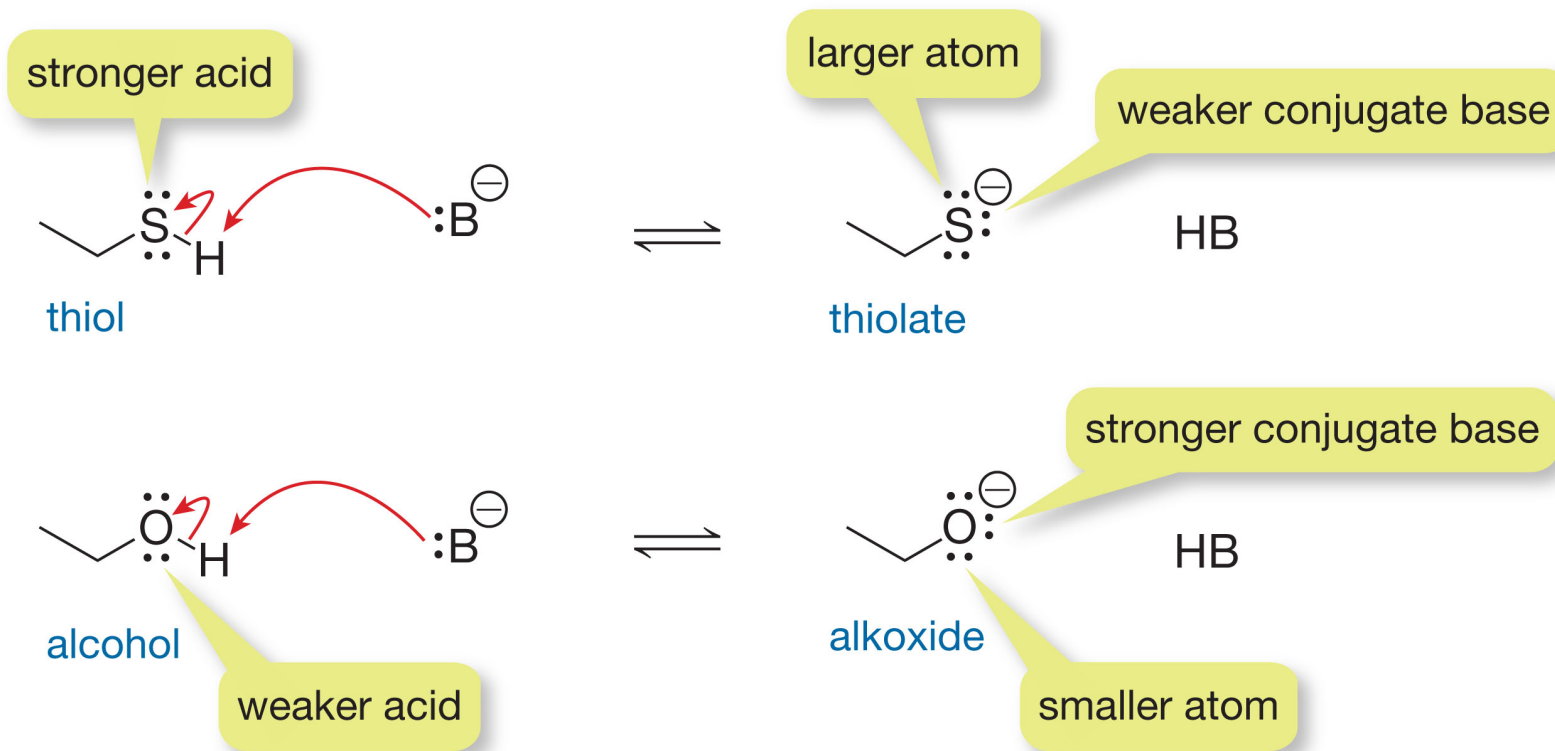


Qualitative Estimates of Relative Acidities

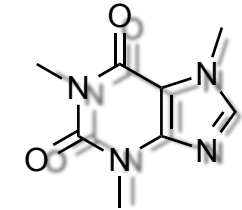


2. Atom Size

- Large atoms can spread charge over larger volumes than small atoms – a negative charge on a large atom is more stable than one on a smaller atom:

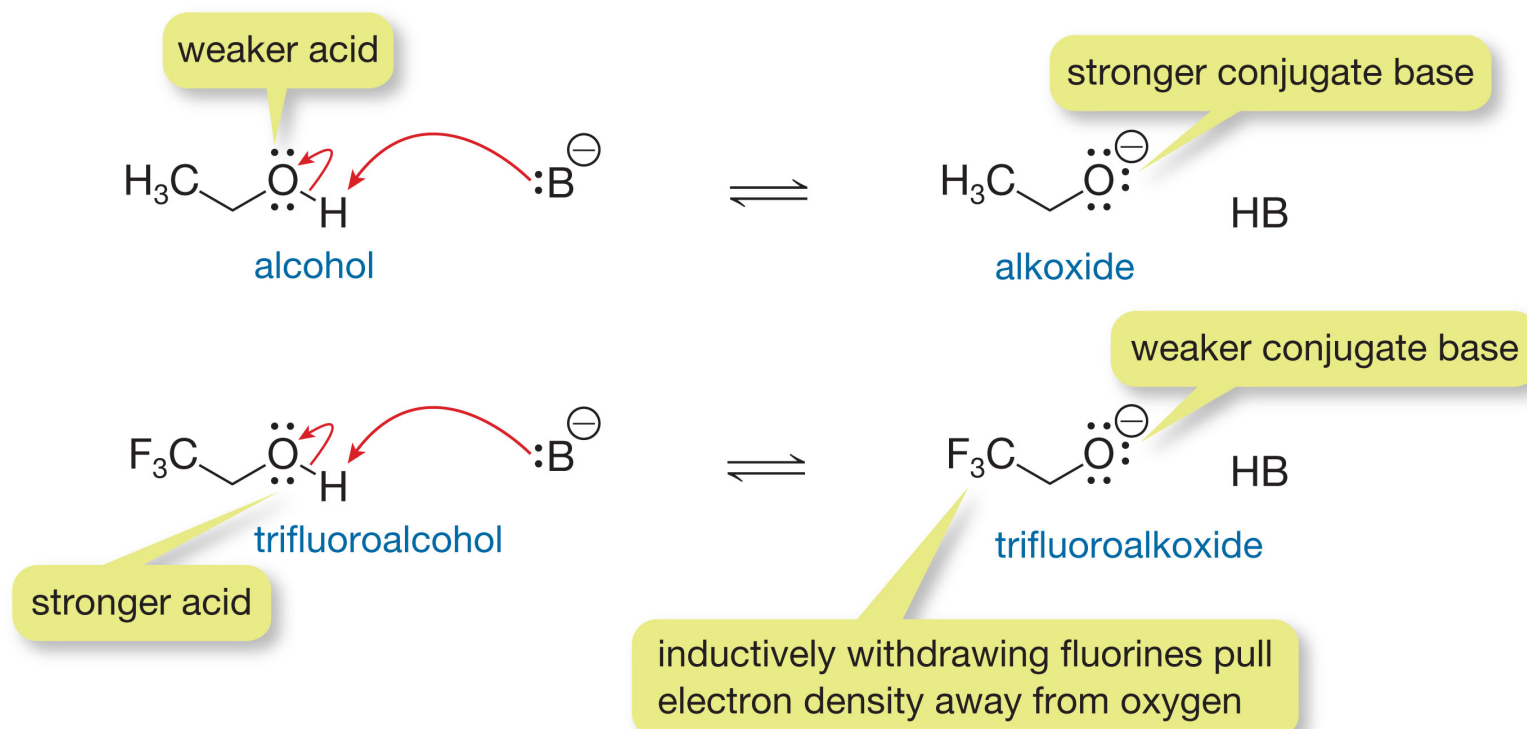


Qualitative Estimates of Relative Acidities

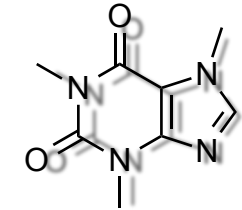


3. Induction

- Bases with their negative charge dispersed over several atoms are generally more stable than bases with localized charge – the presence of electron withdrawing groups (EWGs) near a negative charge can spread out the electrons by *induction*:

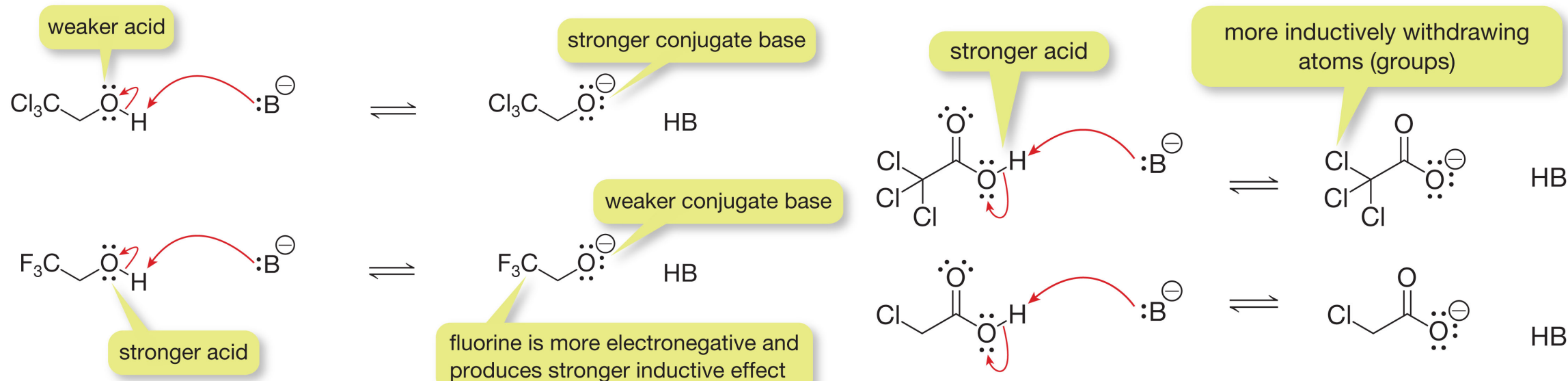


Qualitative Estimates of Relative Acidities

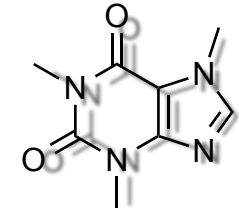


3. Induction

- Induction effects occur through σ bonds.
- The strength of the induction effect depends on the electronegativity of the atoms, the number of atoms, and the distance of the atoms involved.

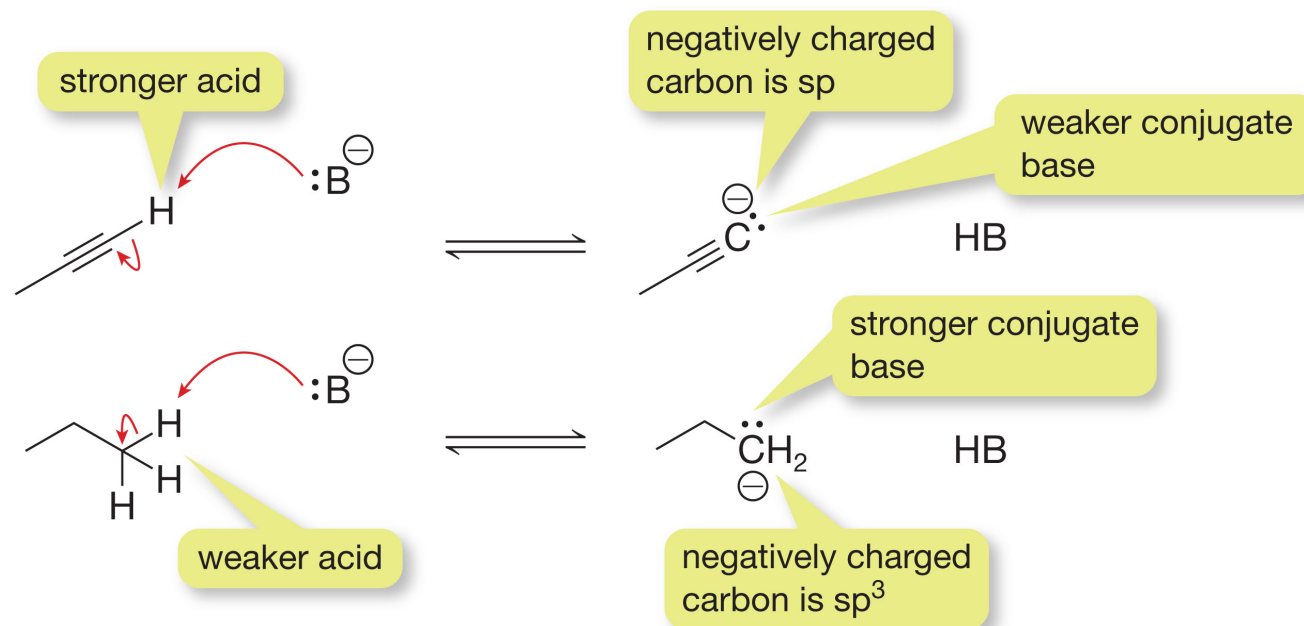


Qualitative Estimates of Relative Acidities

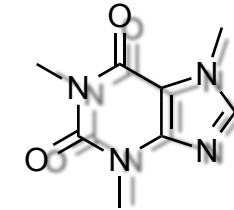


4. Hybridization

- Most organic molecules have their electrons in sp , sp^2 , or sp^3 orbitals.
- Since s orbitals are lower in energy than p orbitals, orbitals with more s -character will be lower in energy and hence more stable.
- A lower energy orbital makes a negatively charged base more stable and hence weaker.



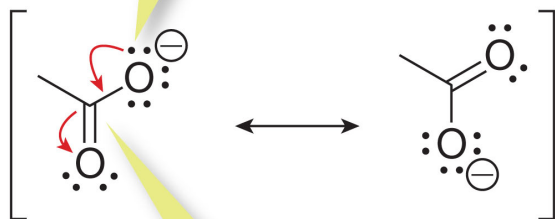
Qualitative Estimates of Relative Acidities



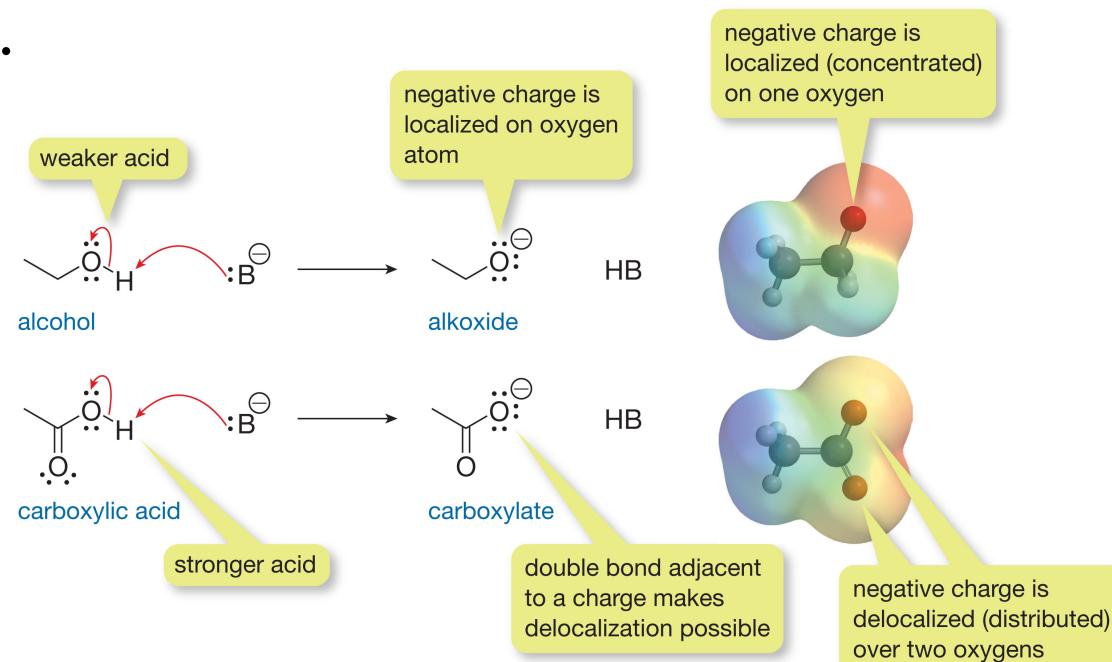
5. Charge Delocalization (resonance)

- Charge delocalization can be a strong stabilizing influence for organic molecules.
- This effect is similar to that of *Induction* except that resonance occurs through the π system of the molecule.

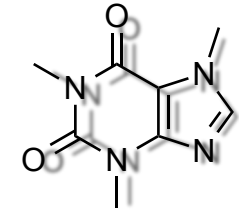
negatively charged oxygen donates an electron pair to form a π bond with carbon



π bond breaks to avoid exceeding the octet rule at the carbon atom

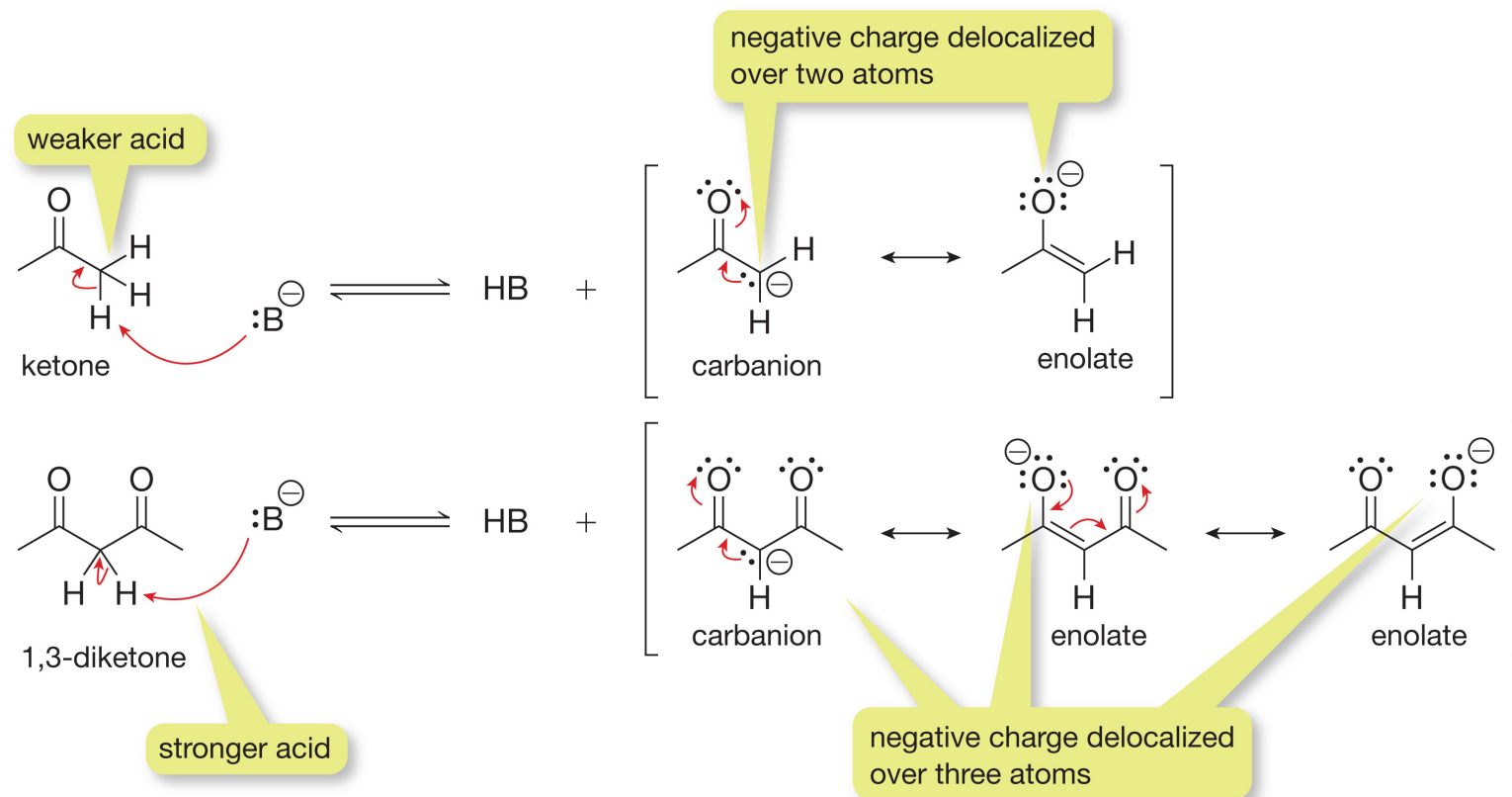


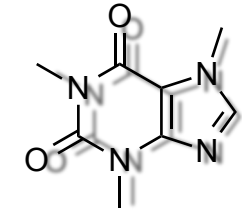
Qualitative Estimates of Relative Acidities



5. Charge Delocalization (resonance)

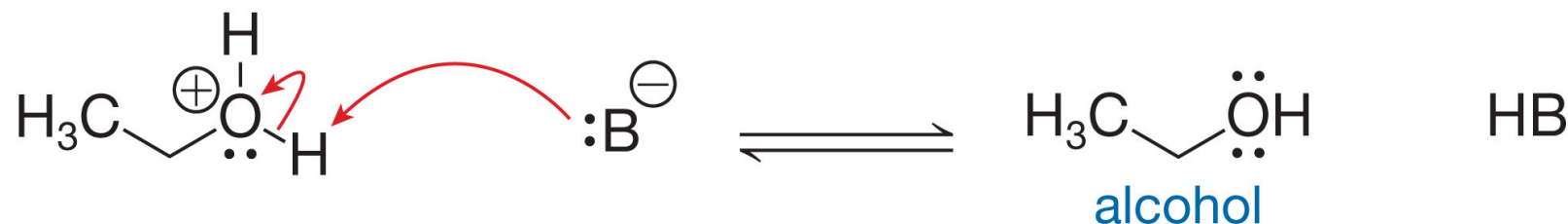
- Many organic reactions involve removing a hydrogen atom from a carbon atom. These reactions can be understood in terms of acid-base reactivity:

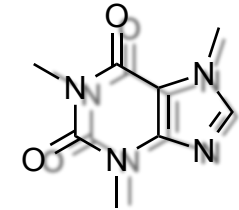




Relative Acidities of (+) Charged Acids

- Organic acids can also be (+) charged.
- To qualitatively assess these we use the same criteria we used for neutral acids, however, in this case we look at the charged acid rather than the charged conjugate base:
 1. Electronegativity
 2. Atomic Size
 3. Induction
 4. Charge Delocalization

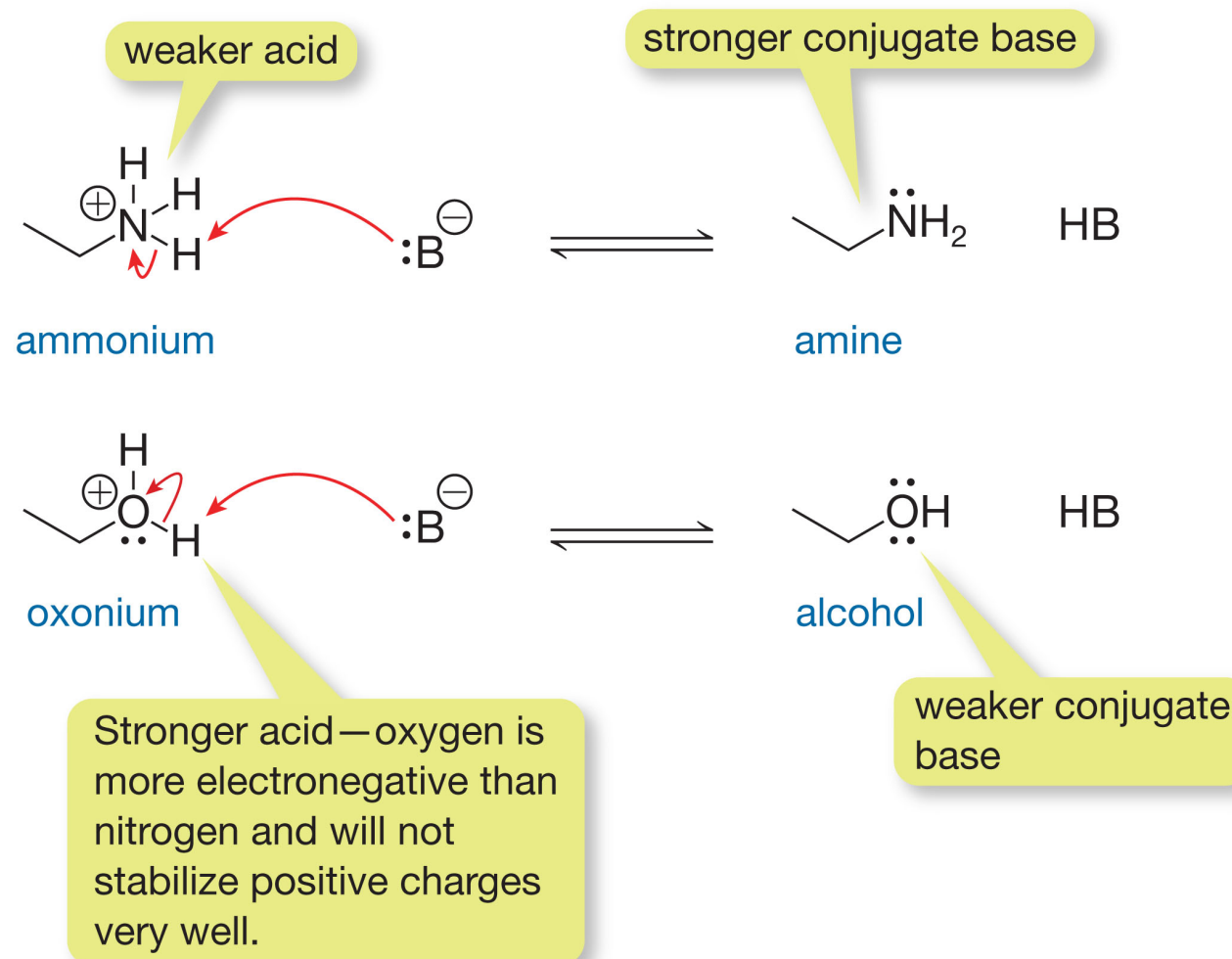


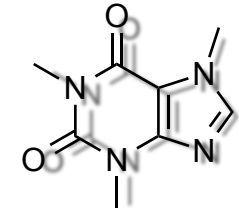


Relative Acidities of (+) Charged Acids

1. Electronegativity

- Electronegative atoms destabilize positive charges, and so acids with positive charge on more electronegative atoms are more acidic, and their conjugate bases are correspondingly less basic:

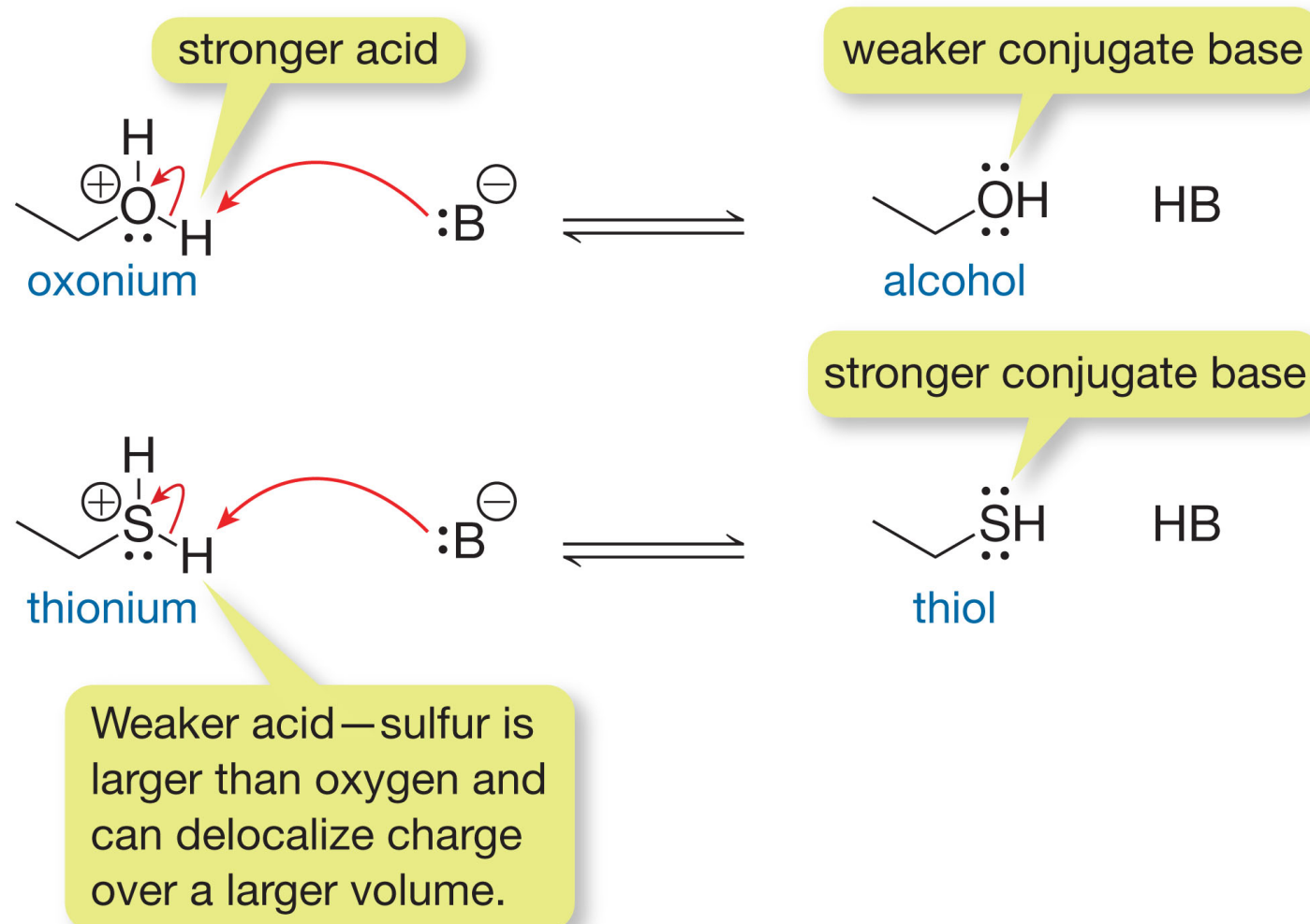




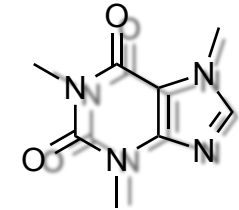
Relative Acidities of (+) Charged Acids

2. Atomic Size

- Large atoms can spread charge over larger volumes than small atoms – a positive charge on a large atom is more stable than one on a smaller atom:

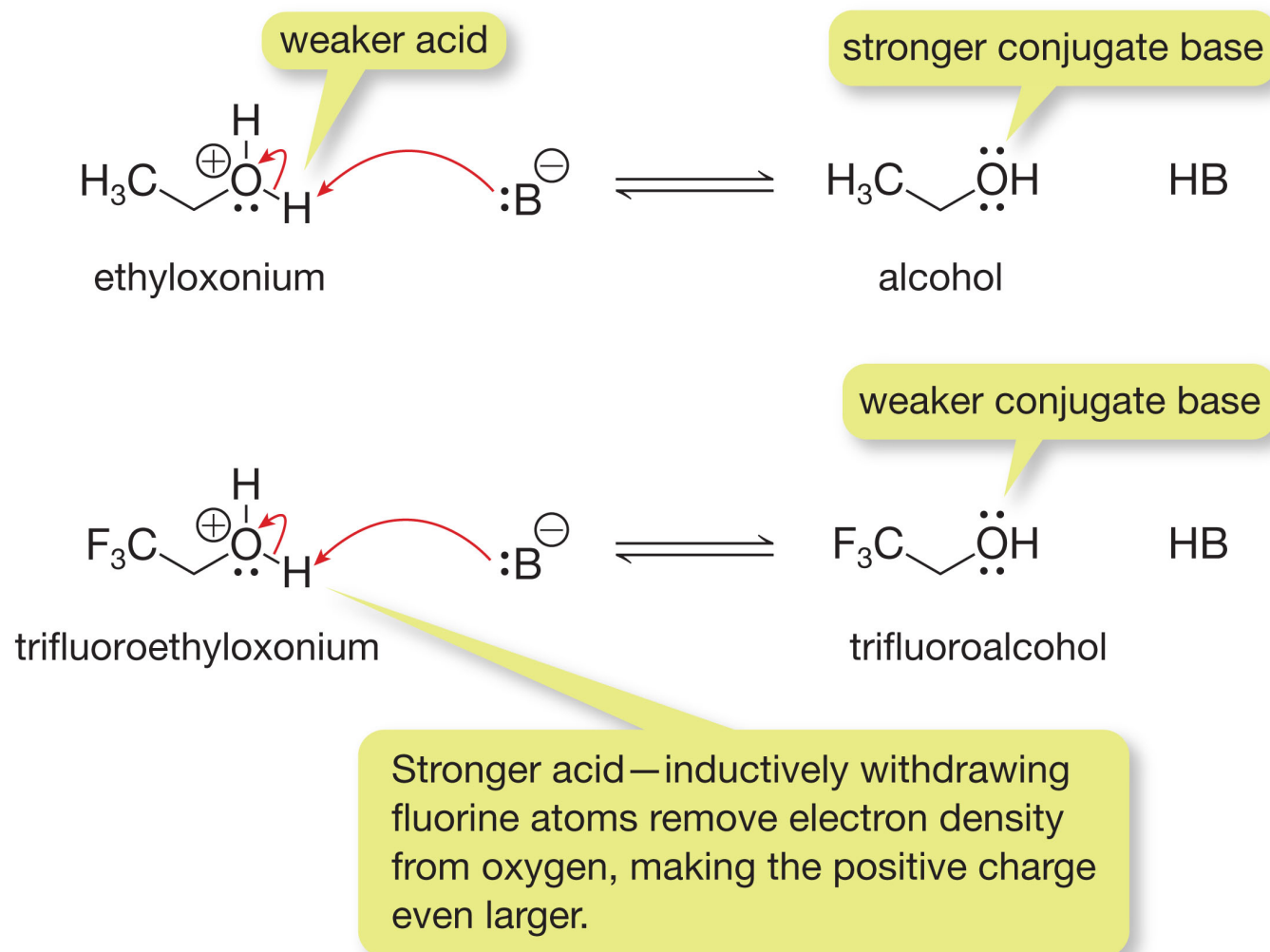


Relative Acidities of (+) Charged Acids

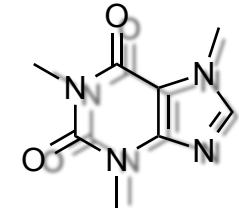


3. Induction

- Nearby electronegative atoms **increase** the effective positive charge on an atom. This effect makes a positively charged molecule **less** stable and therefore a stronger acid:



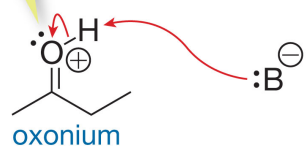
Relative Acidities of (+) Charged Acids



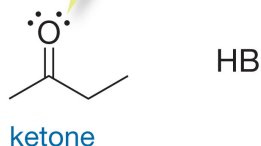
4. Charge Delocalization

- As with negatively charged molecules, delocalization can stabilize positively charged organic compounds by spreading the charge over a larger volume:

Stronger acid—positive charge is less delocalized.

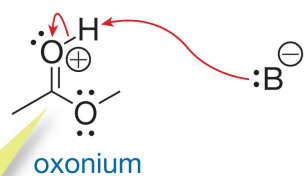


weaker conjugate base

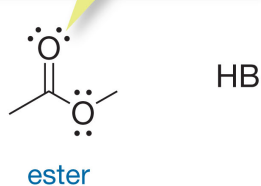


HB

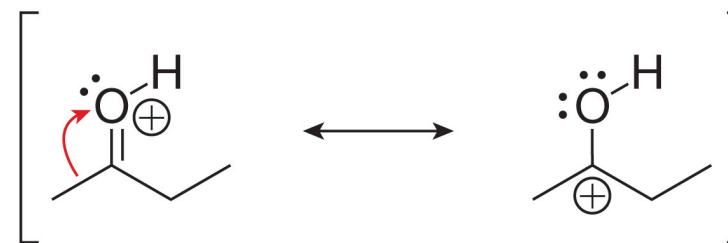
stronger conjugate base



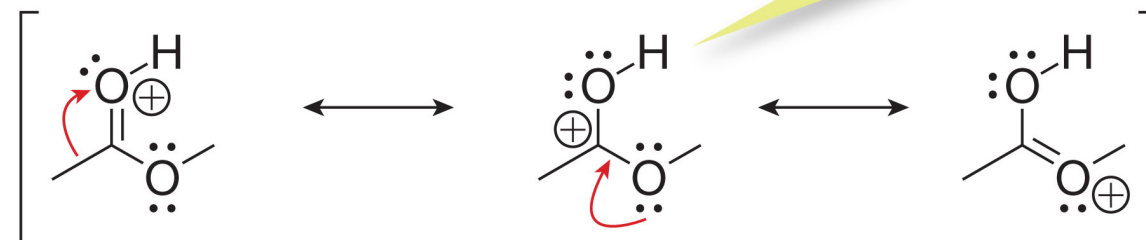
Weaker acid—positive charge is more delocalized.



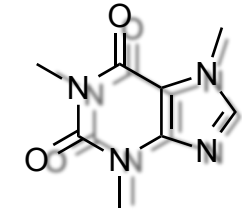
HB



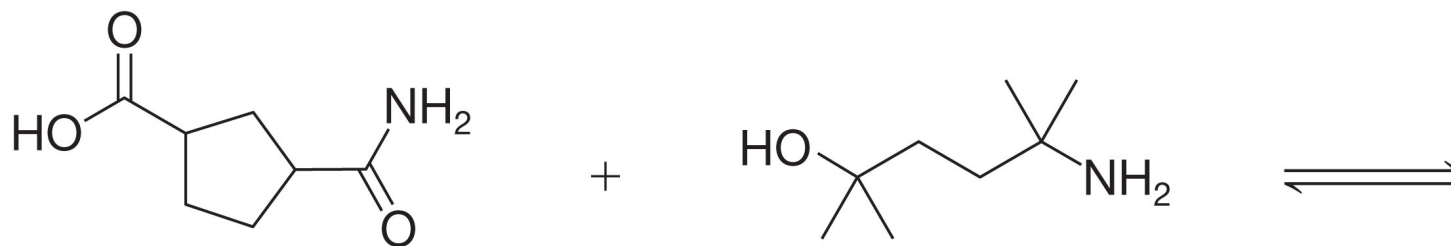
resonance spreads charge over three atoms, resulting in increased stability



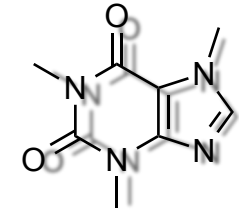
Practice



Predict the most likely acid-base reaction to take place between the following two compounds. Draw a curved arrow mechanism to show the reaction and the products.

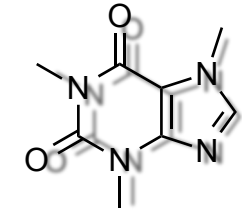


Quantitative Acidity Measurements



- Quantitative acid strength is commonly expressed in terms of the logarithmic acid dissociation constant pK_a .
- A **lower** pK_a indicates a *stronger* acid.
- A **higher** pK_a indicates a *weaker* acid.
- To estimate the pK_a for other functional groups, use the value for the functional group that is the most similar to the structure being examined.

Quantitative Acidity Measurements



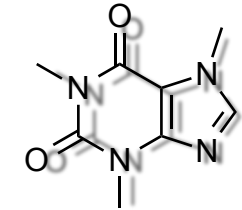
- To estimate the pK_a for other functional groups, use the value for the functional group that is the most similar to the structure being examined.

Acid	Conjugate base	pK_a of acid
		-6
HI H ₂ SO ₄ HBr HCl	I ⁻ HSO ₄ ⁻ Br ⁻ Cl ⁻	< -4
	R-OH	-2 to -4
H ₃ O ⁺	H ₂ O	-1.7
		2 to 5
	Ar-NH ₂	3 to 5
	R-NH ₂	9 to 13
R-SH	R-S ⁻	9 to 12
H ₂ O	HO ⁻	15.7
R-OH	R-O ⁻	15 to 17
R-NH ₂	R-NH ⁻	~ 35

Increasing acid strength

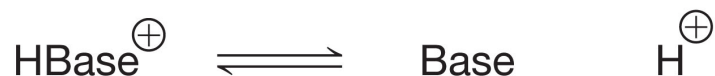
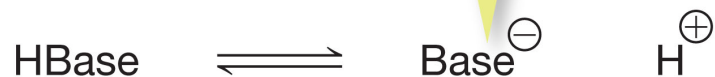
Increasing base strength

Quantitative Acidity Measurements



- Using pK_a to measure base strength:
 - The strength of a base can be quantified using the pK_a of its conjugate acid.
 - In order to identify the correct acid, the acid should always appear as the reactant and the base as a product in the acid-base equilibrium:

when evaluating the strength of a base, write the base on the right side of a pK_a expression



look for the conjugate acid in the pK_a table

when NH_3 acts as a base, use the pK_a of the corresponding conjugate acid, NH_4^{\oplus}



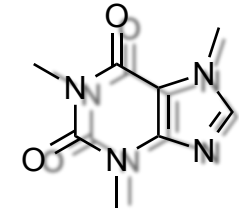
$$pK_a(\text{NH}_4^{\oplus}) = 9.42$$

the base strength of NH_2^{\ominus} is described with the pK_a of the corresponding conjugate acid, NH_3

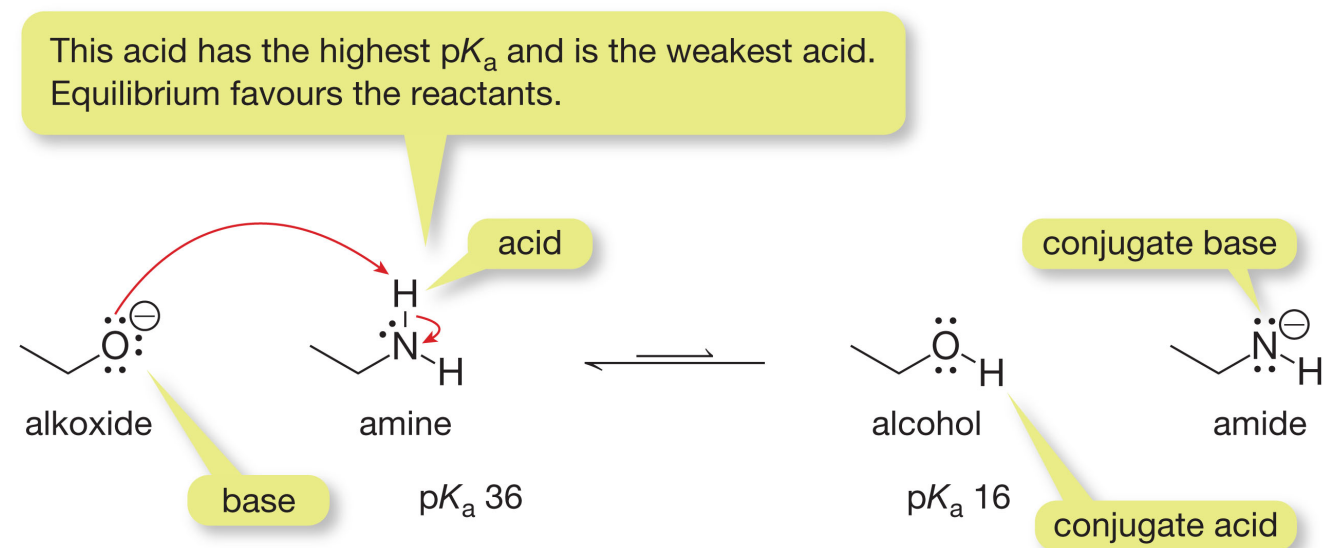


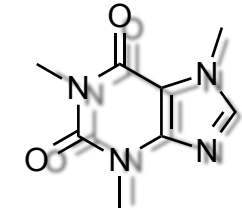
$$pK_a(\text{NH}_3) = 41$$

Predicting Acid-Base Equilibria



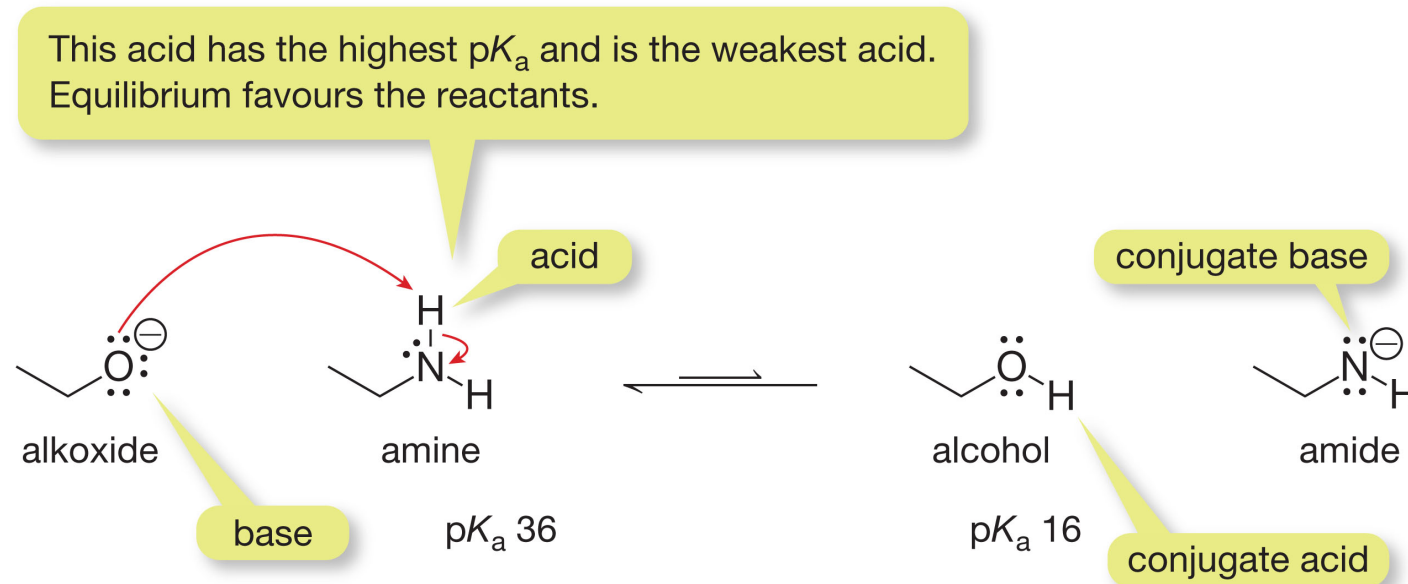
- The behaviour of organic acids and bases when mixed often determines the order in which bonds are broken and formed.
- Equilibrium reactions tend to shift toward the more stable materials.
- *Acid-base equilibria favour weaker acids and bases* – at equilibrium, the concentration of the weaker acid and base is greater than that of the stronger ones.



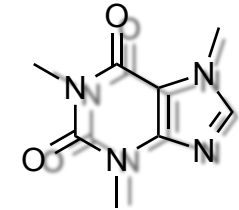


Predicting Acid-Base Equilibria

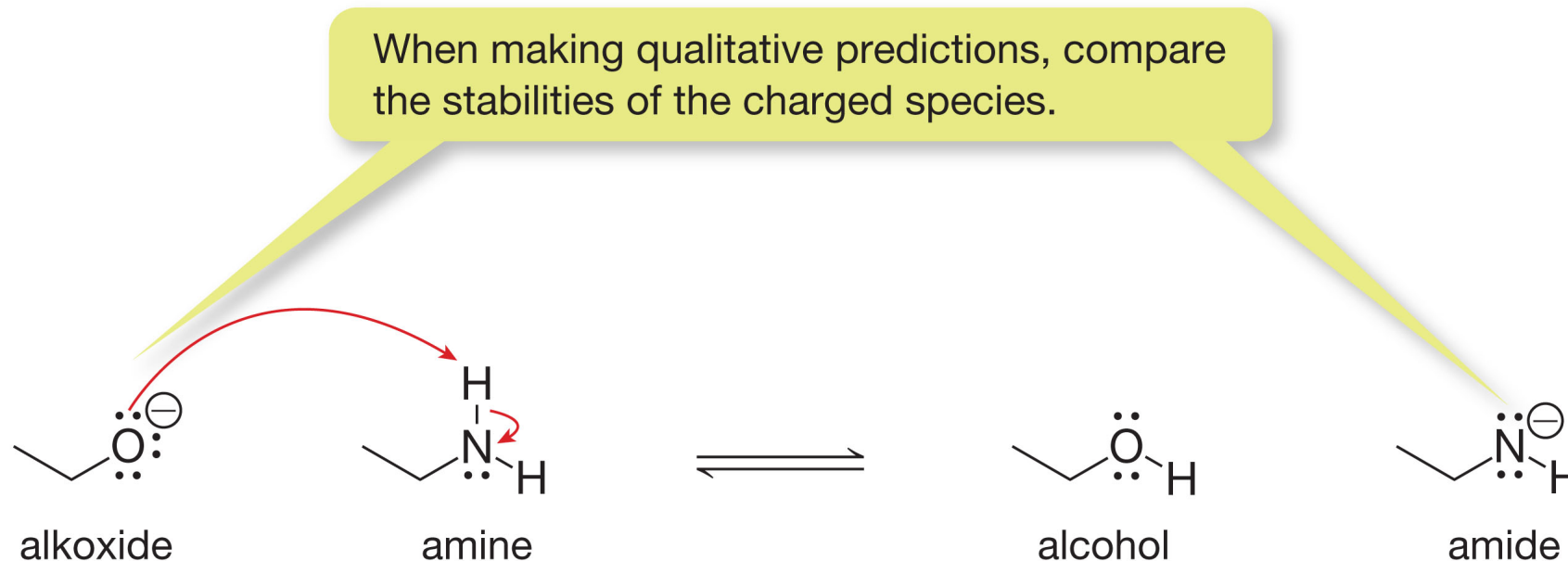
- The difference in pK_a values indicates how *far* the equilibrium shifts.
- Recall that the pK_a scale is logarithmic, therefore each unit of difference represents an order of magnitude (10^1).
- In the example below, the conjugate acid (alcohol) is 20 orders of magnitude (10^{20}) stronger than the acid (amine)!



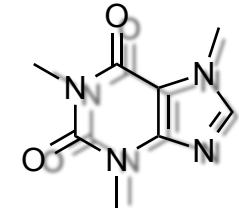
Predicting Acid-Base Equilibria



- Qualitative prediction of equilibria:
 - Since equilibria favour the weaker acids and bases, the *relative* strength of acids and bases can be used to make qualitative predictions about the equilibria.
 - Comparing the stabilities of the charged molecules is the best way to obtain an accurate prediction:

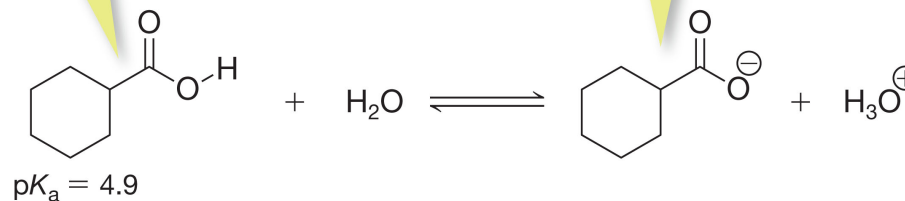


Predicting Acid-Base Equilibria



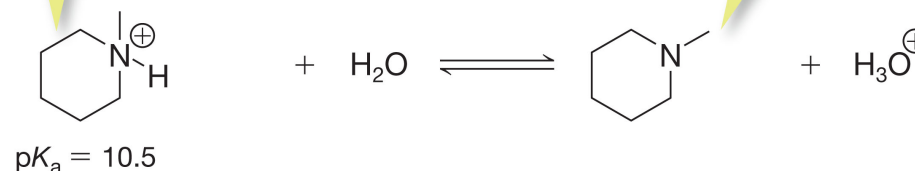
- Protonation states at various pHs:
 - Acids are primarily in their protonated form when the pH is less than the pK_a , and they deprotonate when the pH is greater than the pK_a .
 - If the pH is very close to the pK_a value, a mixture of protonated and unprotonated states will be observed.

If the pH is less than 4.9, the molecules will be in protonated form.

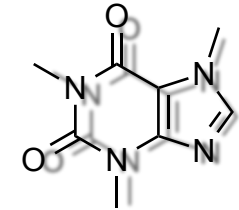


If the pH is greater than 4.9, the molecules will be in the deprotonated form.

If the pH is less than 10.5, the molecules will be in protonated form.



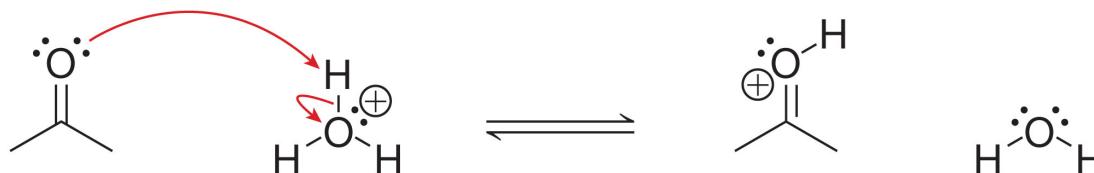
If the pH is greater than 10.5, the molecules will be in the deprotonated form.



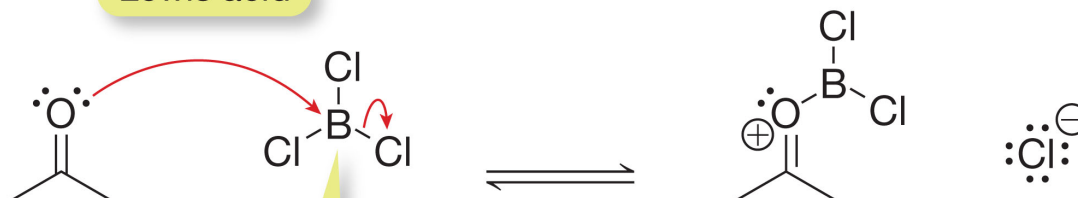
Lewis Acids in Organic Reactions

- **Lewis acids** are defined as *electron pair acceptors*.
- **Lewis bases** are defined as *electron pair donors*.
- Metals are commonly used as Lewis acids, as we will see in later reactions.

Brønsted acid

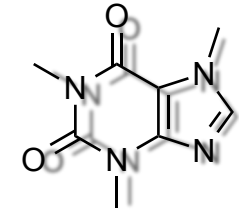


Lewis acid



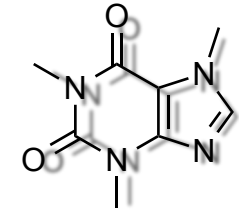
boron has an unfilled octet

Patterns in Acids and Bases



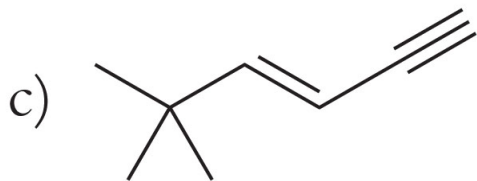
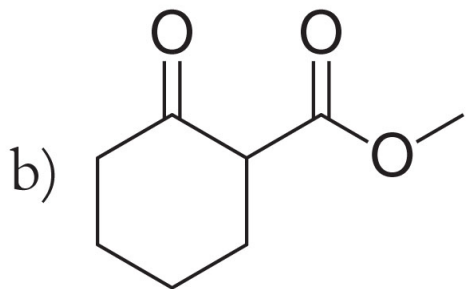
- Periodic trends can be used to quickly estimate the relative strength of acids and bases:
 - When comparing acids and bases, draw complete balanced reactions and compare the *charged components*.
 - When comparing charged atoms within the same row of the periodic table, use electronegativity to determine stability.
 - When comparing charged atoms within the same column of the periodic table, use size to determine stability.
 - Of all the stabilizing factors, electron delocalization (i.e. resonance) is the most profound.

Acid-Base – Practice

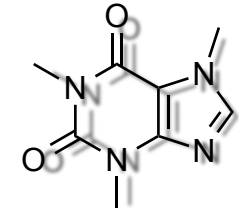


- For each of the following compounds, identify the most acidic proton and then draw a mechanism for its reaction with a strong base, B^- .

6.6

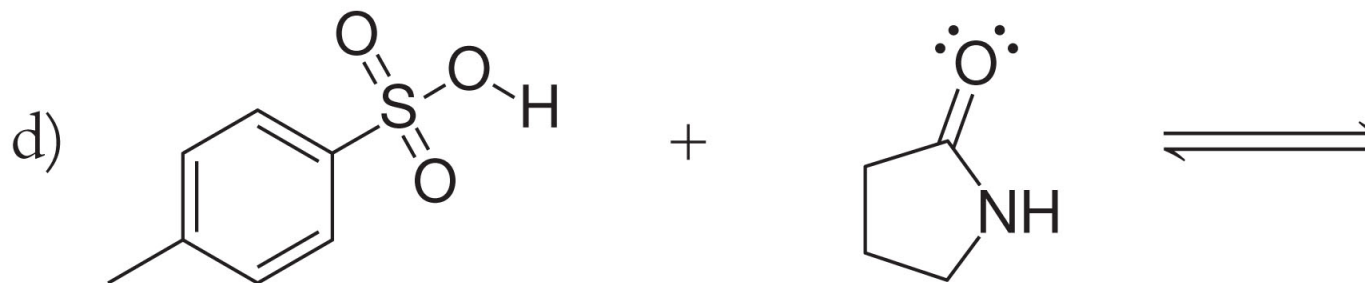


Acid-Base – Practice

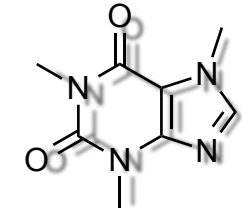


- Predict the products of the following acid-base reactions, and draw a curved arrow mechanism showing their formation.

6.22



Acid-Base – Practice



- Use pK_a data to determine which of the following acids would react with HO^- to yield a reaction that would favour the products.

6.28

