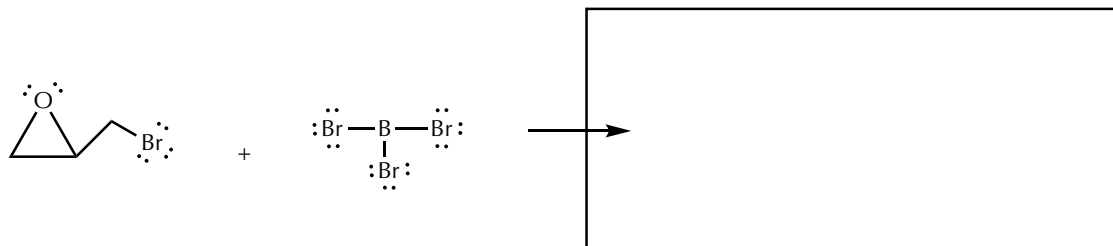
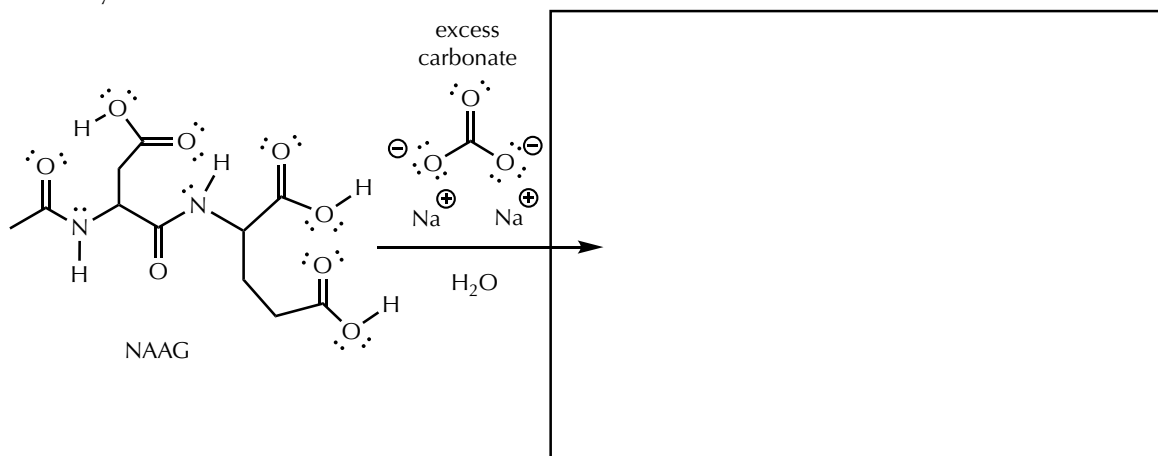


Week 4. There is an exam around the corner! This page, from the Chapter 3 questions 3.34–3.37, give a nice breadth of coverage to Lewis and Brønsted acid-base topics.

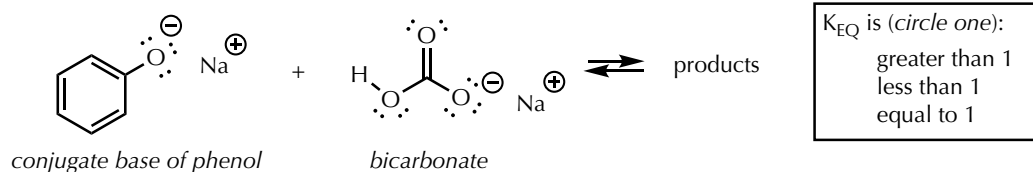
- 3.34 Recalling that ranking Lewis base strengths follows the same trends as ranking Brønsted base strength, predict the product from this highly selective Lewis acid-base complexation reaction.



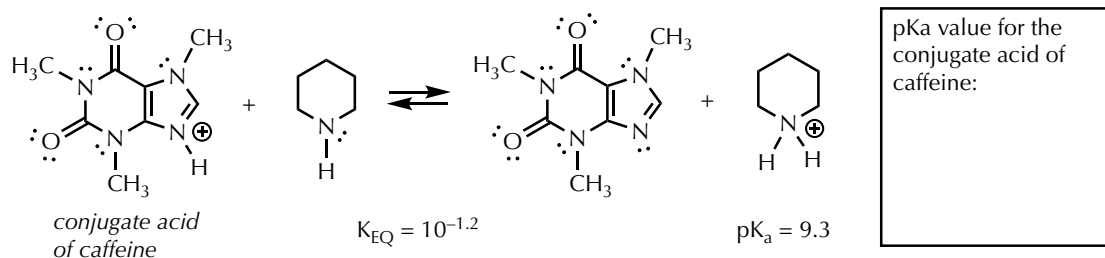
- 3.35 What is the structure of the reaction product between NAAG (one of the most prevalent neurotransmitters in mammals) with excess aqueous sodium carbonate? Give the molecule, derived from NAAG, including any necessary counterions.



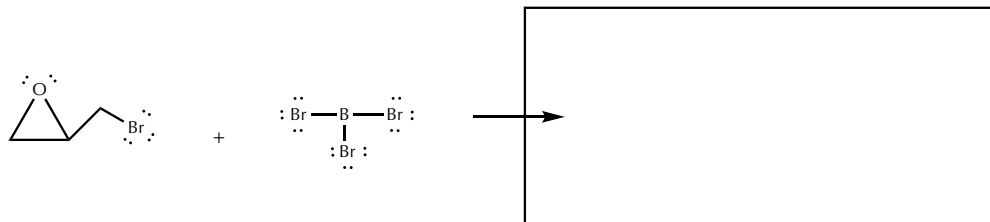
- 3.36 It is possible to use pK_a values to assess an equilibrium constant. Is the value of the equilibrium constant for the 1:1 reaction between conjugate base of phenol and sodium bicarbonate greater than, less than, or equal to 1?



- 3.37 New pK_a values can be determined from measuring the equilibrium constant for an acid-base reaction that is carried out with a reaction partner whose pK_a value is known, and inferring what the pK_a value of the new compound must have been. Based on the following data, what is the estimated pK_a value for the conjugate acid of caffeine?



3.34 Recalling that ranking Lewis base strengths follows the same trends as ranking Brønsted base strength, predict the product from this highly selective Lewis acid-base complexation reaction.



Acid-base chemistry provides a critical foundation for all of the future studies in organic chemical reactivity.

All of the previously established principles for evaluating molecular structures (closed shell atoms, charges and charge placement, electronegativity difference, delocalization, geometry, atom size difference) are used to explain observed chemical reactivity across a diverse array of experimental results. Nearly all of the examples used to create exam questions are not “made up,” but rather derive from actual published reports in the contemporary chemistry journals.

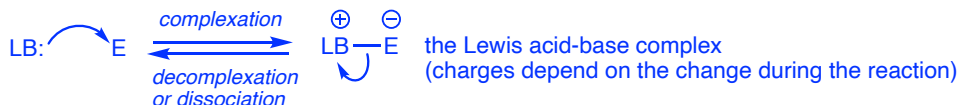
The Lewis acid-base chemistry of open shell atoms is not surprising: atoms with open shells will react to give their best (most stable) closed-shell arrangement.

The text for part (a) indicates (i) a Lewis acid-base complexation reaction and (ii) that it is highly selective. At this point in CHEM 210, only two reactivities have been introduced: Lewis acid-base complexation reactions and Brønsted acid-base reactions. The text of this problem is doing the identification for you, and so these words are intended to focus your attention on “Lewis acid-base complexation” and what this means. And that is fine, but you need to know what that means, and what you anticipate about what sorts of decisions need to be made, because you cannot figure it out from the information provided. The question, in other words, is testing whether you have figured out two things: (i) what “Lewis acid-base complexation” means, and (ii) how to evaluate a choice (i.e., that something is “highly selective” means that you are about to be presented with a choice.

Lewis acid-base complexation

You should be anticipating that there is at least one open shell atom (the Lewis acid, an electron pair acceptor) and a reactive partner that has a non-bonding electron pair that it can share (the Lewis Base, an electron pair donor). The competition could be between a set of different open shell atoms, or the competition could be between a set of different electron pair donors, or both.

open shell atom: “E” (a Lewis acid, accepts an electron pair, to share, and makes a bond)
 an atom with a nbe pair to share: “LB:” (a Lewis base, donates an electrons pair, to share, and makes a bond)



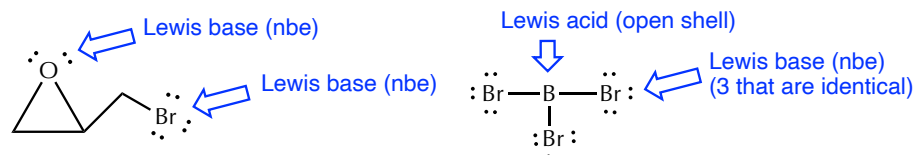
Competition and selectivity

When there are competing reactions, it turns out that there are a number of different ways to predict which pathway is the most likely, and so what is the most likely outcome. These criteria might include relative statistics (there is more of one outcome than another), relative rates (how much faster is one outcome than another), or relative stability (how much more stable is one outcome than another).

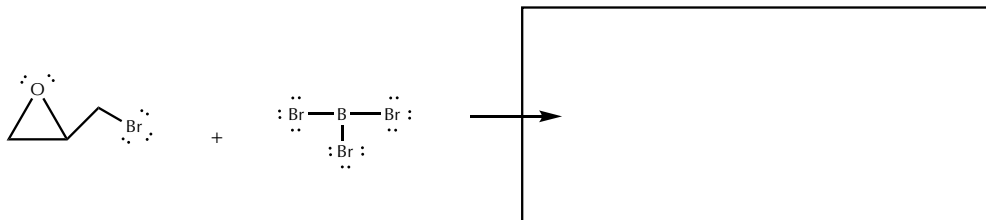
Evaluating relative stability is the first type of criterion that is part of CHEM 210.

So, in summary: before you even look at the example, you are anticipating from the text of the question that there are going to be different outcomes from reactions between one open shell atom and at least two different atoms with nbe pairs to share, or between one atom with nbe to share and at least two different open shell atoms, or more than one of each. And you anticipate needing to evaluate the relative stability of the possible outcomes.

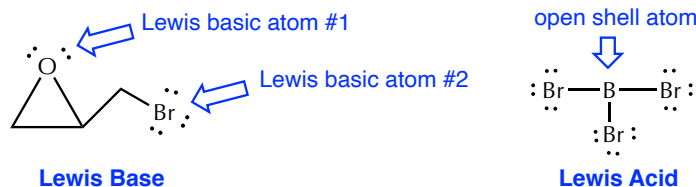
Looking at the two molecules, you see three distinctive atoms with nbe pairs (potential Lewis bases) and one atom that has an open shell.



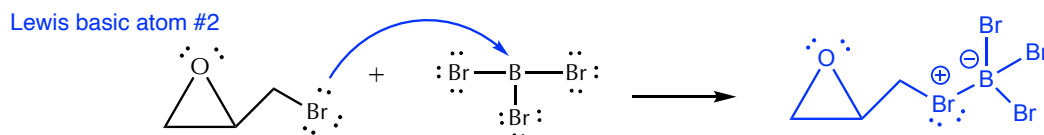
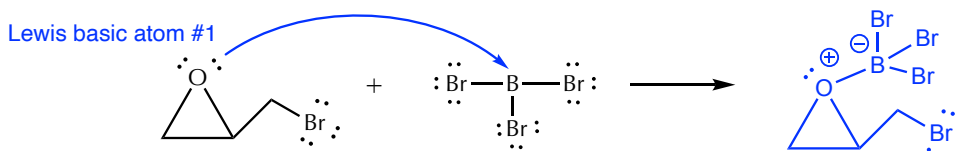
3.34 Recalling that ranking Lewis base strengths follows the same trends as ranking Brønsted base strength, predict the product from this highly selective Lewis acid-base complexation reaction.



With only one open shell atom in these two molecules, the one with the boron atom is going to serve as the Lewis acid (with the boron atom being the Lewis acidic atom). That means that competition is between the oxygen atom and the bromine atom, in the other molecule serving as the Lewis base.



All of the previous lessons from the course apply (behavior of well-behaved atoms; curved arrow convention, including using it to predict reactivity; assignment of formal charges) and can be used to predict the two outcomes for comparison.



How to make the choice between these two outcomes?

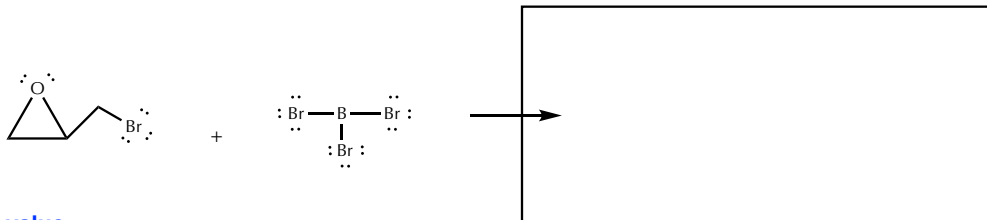
One of the core lessons from acid-base chemistry relates to science, in general: if you have competing factors with no generalization for ranking them, then you need to rely on experimental results.

As described earlier, all of the usual molecular features apply to evaluating stability: closed shell atoms, charges and charge placement, electronegativity difference, delocalization, geometry, atom size difference. When more than one of these factors are in competition, there is no universal ranking of which is more or less important, and so the experimental results are needed (or, a set of representative experimental results are needed, from which to create an analogy).

Lewis acid-base chemistry overlaps with Brønsted acid-base chemistry because all Brønsted bases are Lewis bases, and *vice versa*. The pK_a table, which summarizes experimental results for Brønsted acid strength, also summarizes Brønsted base strength, and so, too, Lewis base strength. And the evaluation of acid-base strength, at least at this point in the course (and, in fact, in general) is built upon relative stabilities.

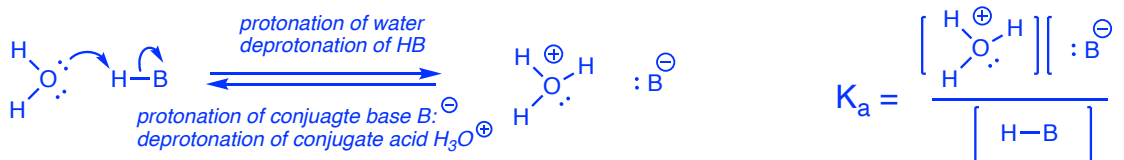
So, the only way to make the choice between these two outcomes is to understand how to apply the information from the pK_a table to the evaluation of the two different Lewis basic atoms #1 and #2.

3.34 Recalling that ranking Lewis base strengths follows the same trends as ranking Brønsted base strength, predict the product from this highly selective Lewis acid-base complexation reaction.

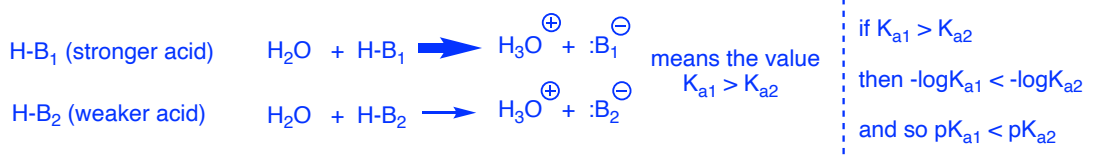


The pK_a value

For a given Brønsted acid (H-B; meaning any covalent bond involving a hydrogen atom), the standard acid strength is defined by its ability to protonate water, which is used as the point of reference (the “a” in pK_a).



If you are comparing two Brønsted acids (H-B₁ and H-B₂), you need to understand that being “a stronger acid” means that the reaction with water (shown above) is more likely to happen. In chemistry terms, that means that the reaction of a stronger acid lies more to the right than it does for a weaker acid. If the reaction of H-B₁ lies more to the right (stronger acid) than it does for H-B₂ (weaker acid), then the K_a for H-B₁ (K_{a1}) will be a greater value than the K_a value for H-B₂ (the weaker acid does not give up its proton as readily, so there will be relatively less “H₃O⁺ and B₂⁻” formed, compared with “H₃O⁺ and B₁⁻” and less H-B₁ relative to the concentration of H-B₂).



ITEM I: for two acids, H-B₁ and H-B₂ if H-B₁ is the stronger acid, it has the lower pK_a value

The relative Brønsted base strengths of the conjugate bases can be evaluated, also, because a stronger acid (the H-B₁ bond is more likely to break, and so B₁⁻ part of H-B₁ releases its proton) creates a corresponding conjugate base (B₁⁻) that does not bond with a proton as well, and is classified as the weaker conjugate base (B₁⁻) relative to the conjugate base (B₂⁻) derived from a weaker acid (H-B₂), which is more inclined to keep its H-B bond intact.

ITEM II: for two acids, H-B₁ and H-B₂ if H-B₁ is the stronger acid, it has the weaker conjugate base B₁⁻

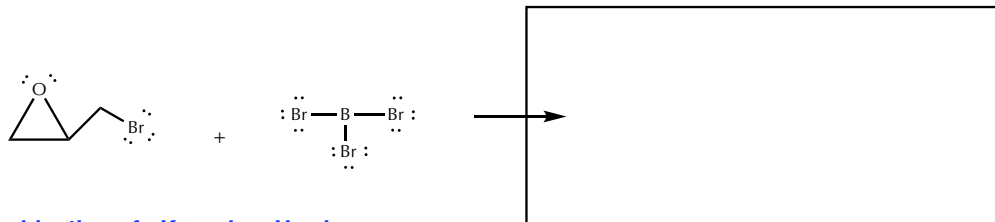
Thus, when you need to compare the relative base strength of two bases, you can use the comparison of the pK_a values of their conjugate acids. For two bases, B_x⁻ and B_y⁻, if the pK_a value of their conjugate acids is $pK_{ax} > pK_{ay}$, then H-B_x is a stronger acid than H-B_y, and so B_x⁻ is a weaker base than B_y⁻. There is no exception to these relationships, and so every pairing can be assessed exactly the same way. Take any random pair of molecules whose pK_a values are known, you can say something about their relative acidities. For example: the pK_a of ethanol (CH₃CH₂OH) is 17 and the pK_a value of ethanethiol (CH₃CH₂SH) is 10.2.

Ethanethiol is a stronger Brønsted acid than ethanol (10.2 < 17).

You can also compare relative base strengths, but you need to be careful to select the corresponding conjugate acids for doing the evaluation. For example, if you want to compare the relative Brønsted basicity of hydroxide (HO⁻) and ethoxide (CH₃CH₂O⁻), then you (a) need the pK_a values of their conjugate acids (the conjugate acid of hydroxide is water, H₂O, which has a pK_a value of 15.7; the conjugate acid of ethoxide is ethanol, CH₃CH₂OH, which has a pK_a value of 17). Because water has a lower pK_a value than ethanol (15.7 < 17), then water is the stronger conjugate Brønsted acid of the pair of bases, therefore hydroxide is a weaker base than ethoxide. The stronger base (ethoxide) has the weaker (higher pK_a) conjugate acid.

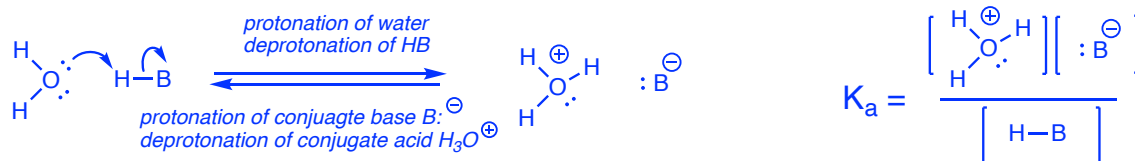
ITEM III: for two bases, B₁⁻ and B₂⁻ if B₂⁻ is a stronger base, the pK_a of its conjugate acid (H-B₂) will be higher (a weaker acid) than that of H-B₁

3.34 Recalling that ranking Lewis base strengths follows the same trends as ranking Brønsted base strength, predict the product from this highly selective Lewis acid-base complexation reaction.

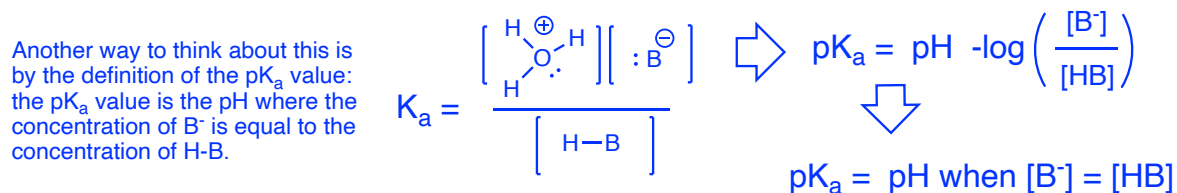
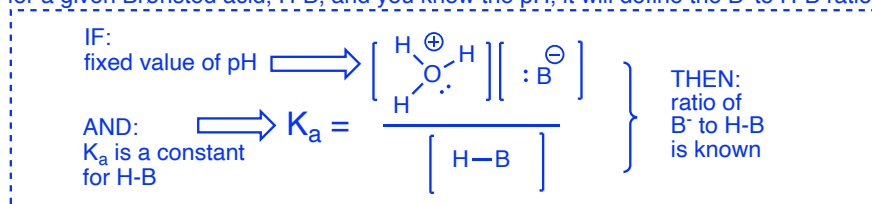


The combination of pK_a and a pH value

The K_a relationship is also used in another way: to make an estimate of the B^- to H-B ratio at a given pH (concentration of H_3O^+) value. Starting with a duplication of exactly the same relationship and definitions:



Experimentally, it is possible to create a solution with a defined pH value (this is a buffer). That means if you know the K_a for a given Brønsted acid, H-B, and you know the pH, it will define the B^- to H-B ratio.



That is: when you know the pK_a value, then at any given pH, you can estimate the ratio of B^- to H-B (and at the pH corresponding to the pK_a , that ratio is exactly 1, i.e., $[B^-] = [H-B]$). As you move to the pH values that are in the more acidic direction (lower the pH of the environment), then there is more of the acid form (H-B), the ratio increasing by a power of ten for every pH unit. As the pH changes in the more basic direction (higher pH), then the base form (B^-) dominates. As an example, Ph-NH₃⁺ (from the pK_a table) has a pK_a value of 4.6. By definition, in a solution of pH = 4.6, there should be a 1:1 ratio of the acid to its conjugate base. The ratio will change by a power of ten for every pH unit above and below 4.6. This concept is true for any pK_a value. Molecules with more than one acidic proton can be handled as a series of independent cases.

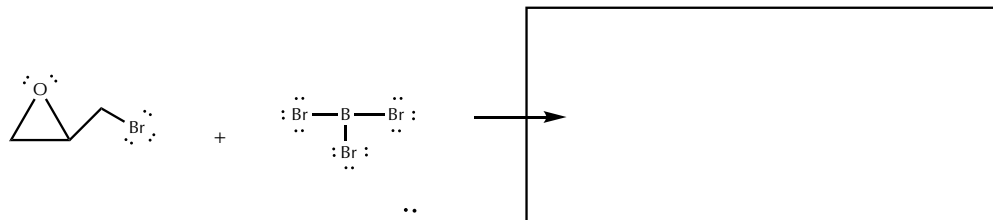
pH	acid form (HB)	base form (B^-)
9.6	1	100,000
8.6	1	10,000
7.6	1	1,000
6.6	1	100
5.6	1	10
4.6	1	1
3.6	10	1
2.6	100	1
1.6	1,000	1
0.6	10,000	1

And this is exactly the story that the equation tells:

$$4.6 = pH - \log\left(\frac{[B^-]}{[HB]}\right) \Rightarrow 4.6 = 2.6 - \log\left(\frac{[B^-]}{[HB]}\right) \Rightarrow 4.6 = 2.6 - \log\left(\frac{1}{100}\right)$$

(1) take a molecule with pK_a 4.6 (2) put it in a solution of pH 2.6 (3) the [HB] to $[B^-]$ ratio is 100:1

3.34 Recalling that ranking Lewis base strengths follows the same trends as ranking Brønsted base strength, predict the product from this highly selective Lewis acid-base complexation reaction.

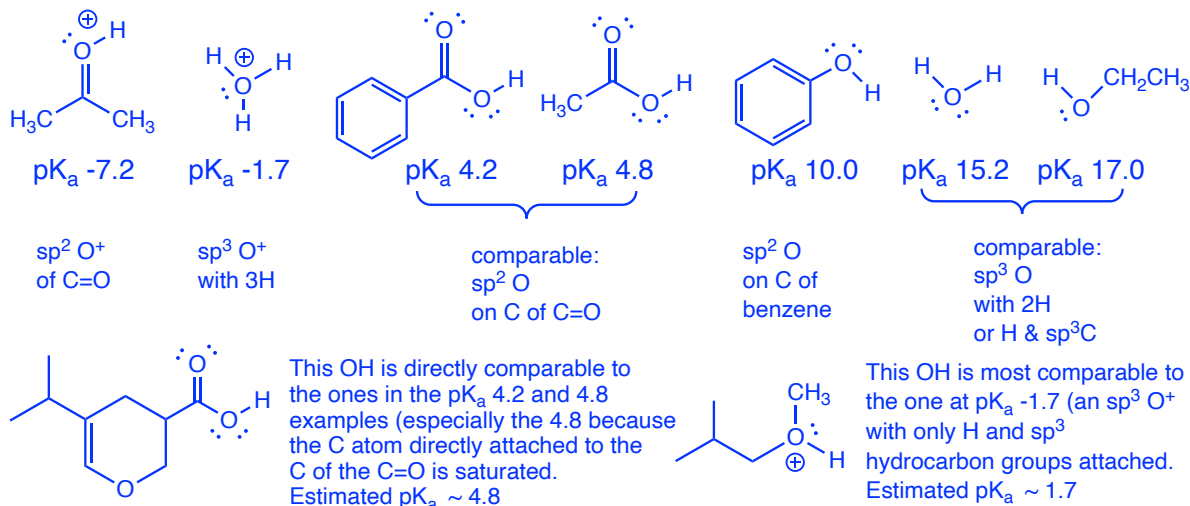


Using the pK_a table for making pK_a estimates: analogies between structurally similar compounds

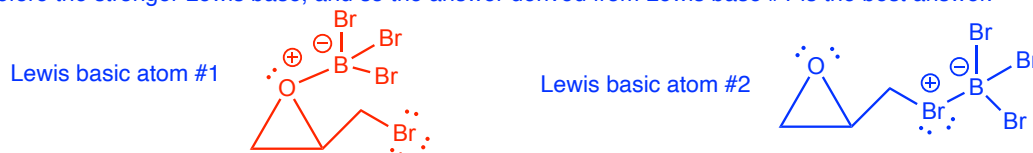
With millions of known organic molecules, the examples in any given pK_a table will always be limited, so learning how to create good analogies and comparisons is critical. In general, molecules with the same functional group will have comparable pK_a values for that functional group if (and only if) the structural setting of that functional group is as comparable as possible, meaning all of its identifiable structural features, and particularly (a) the identity of the atom, (b) the hybridization, (c) the charge, (d) the directly attached organic structure (including its identity, hybridization, charge, delocalization, and so on).

The only differences that can generally be assumed to be small are the structural effects of a directly attached hydrogen atom relative to simple, saturated hydrocarbon chains (-H, -CH₃, -CH₂CH₃, -CH(CH₃)₂, -CH₂CH₂CH₃, etc, and including rings that are only made up of saturated carbon atoms in the positions nearby to the potential Brønsted acid).

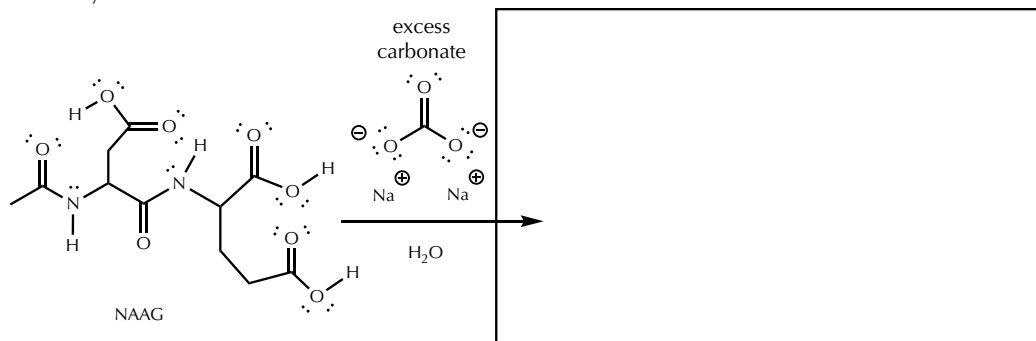
Selecting the proper analogy is critical, because small structural variation can lead to large differences in acidity. There are example of "OH" groups on the CHEM 210 pK_a table that range from -9 (sulfuric acid) to 17 (ethanol), which is a range of 10^{26} difference in acid strength. Take just a few of the "OH" examples:



And that brings back the original question! Which of the Lewis basic atoms is the stronger Lewis base? The oxygen atom (base #1) or the bromine atom (base #2)? The pK_a table lacks the most direct comparison for these two as bases. Although an sp^3 O as a base is present twice (water, ethanol), there is no example of an uncharged bromine atom (or any other halogen, for that matter) acting as a base to give a cationic bromine atom. And when you think about the conjugate acids that you might compare: H₃O⁺, pK_a -1.7 from the water would need to be put up against, for instance H₂Br⁺ as an sp^3 Br⁺ reference. And because UNCHARGED HBr (pK_a -7 to -9) is already more acidic than H₃O⁺, then uncharged sp^3 Br is much less basic than uncharged sp^3 O. The sp^3 O is therefore the stronger Brønsted base, and therefore the stronger Lewis base, and so the answer derived from Lewis base #1 is the best answer.



3.35 What is the structure of the reaction product between NAAG (one of the most prevalent neurotransmitters in mammals) with excess aqueous sodium carbonate? Give the molecule, derived from NAAG, including any necessary counterions.



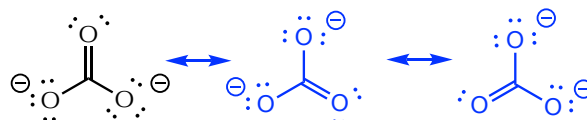
Predicting Brønsted acid-base reactions

In part (b), a typical “predict the product(s)” question is asked explicitly (and the format is clearly indicating it). The number of possible reactions to select from, at this point in the course, is limited (Lewis acid-base and Brønsted acid-base). The Lewis acid-base (as in part a) can be rapidly excluded because there are no open shell atoms present, and so this is a prediction about a Brønsted acid-base reaction. One of the reagents will be the Brønsted acid (proton donor) and the other will be the Brønsted base (proton acceptor). One of the reagents is indicated as being in excess, and this would generally mean that there is more than one reaction taking place. As in part a, the possible sites for the Brønsted acid-base reactions need to be assessed.

The **NAAG** molecule has many different atoms whose Brønsted acidity can be assigned. Indeed, the molecule is filled with bonds to hydrogen atoms and, in principle, all of them can be considered. The pK_a table can be used to assign estimated pK_a values to these potential Brønsted acids. There are also plenty of atoms with lone pairs, and every one of them is a potential Brønsted base.

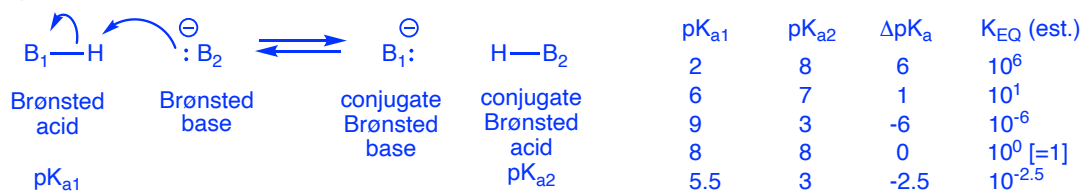
Taking in the landscape of a question rather than just jumping into the details is generally useful.

When you look at sodium carbonate, the question of which partner is going to be the Brønsted acid and which is going to be the Brønsted base is quickly settled, because sodium carbonate has no protons and therefore cannot possibly serve as a Brønsted acid. In addition, there is not even a choice to make about which is the Brønsted basic atom, because all three oxygen atoms are actually identical (recall that being aware of delocalization needs to be an automatic part of considering molecular structures, and carbonate has three equally significant resonance contributors).

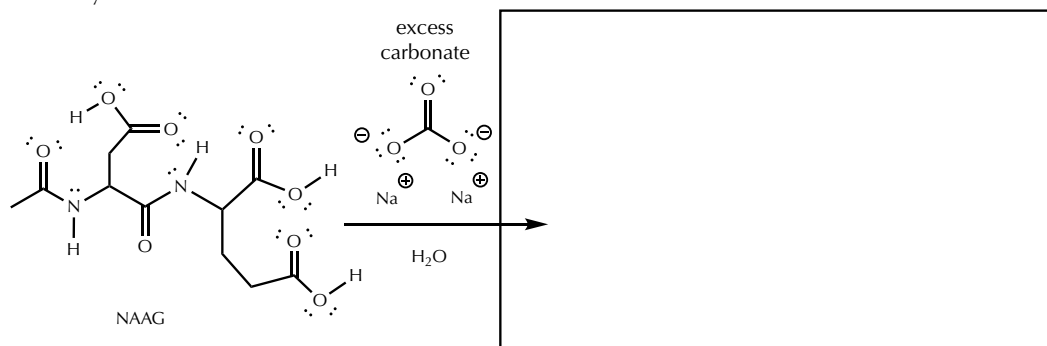


The Brønsted acid-base reaction is a single process that can be observed in millions of different molecular combinations. Every covalent bond associated with a hydrogen atom is a potential Brønsted acid, and every atom (or set of atoms) with an electron pair to share, and form a new bond, is a potential Brønsted base.

The degree to which a Brønsted acid-base reaction will take place can be estimated by the relative difference in the pK_a values. There are constraints on this method of estimating, because there are factors such as relative amounts that can effect an experimental outcome, but the method is a good start for deciding whether a reaction will lie to the left or the right, and by about how much. Because the weaker acid has the stronger bond to hydrogen, the Brønsted acid with the higher pK_a value is expected to be favored. And because pK_a values are the exponents associated with the K_a equilibrium constant, a rough estimate of the equilibrium constant (for the one to one mixture of the reagents) can be made from the difference in the pK_a values. Keep the math in mind: if the pK_a of the product acid is higher (weaker), then it will predominate at equilibrium, and the equilibrium constant will be greater than 1. If the starting material's pK_a is higher, on the other hand, the reaction will lie to the left, and the equilibrium constant will be a fraction.



3.35 What is the structure of the reaction product between NAAG (one of the most prevalent neurotransmitters in mammals) with excess aqueous sodium carbonate? Give the molecule, derived from NAAG, including any necessary counterions.

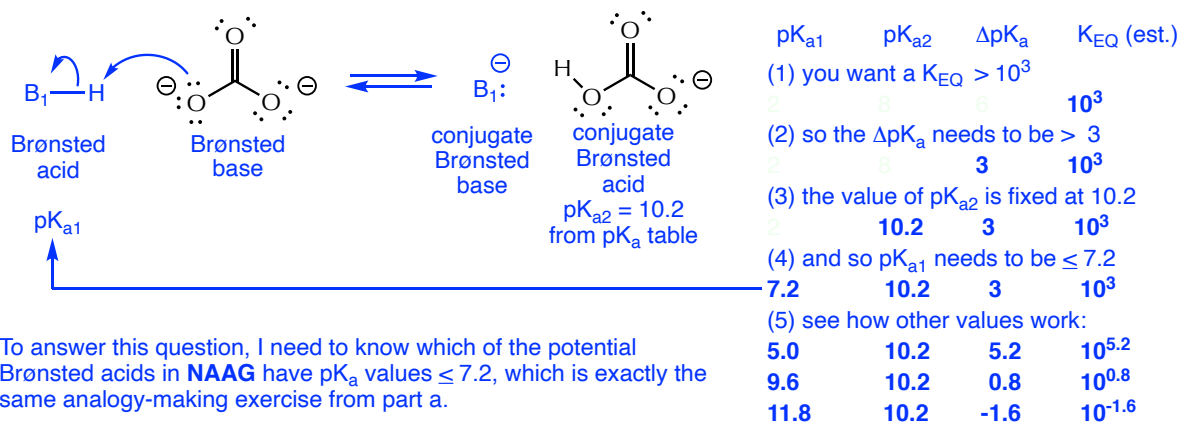


Predicting Brønsted acid-base reactions

For answering this question, the magnitude of the equilibrium constant that qualifies as a completed reaction is needed. The question does not state one, and so there must be a general guideline that is a part of the course. This might come from class; it might appear elsewhere on the exam paper, in a set of general guidelines.

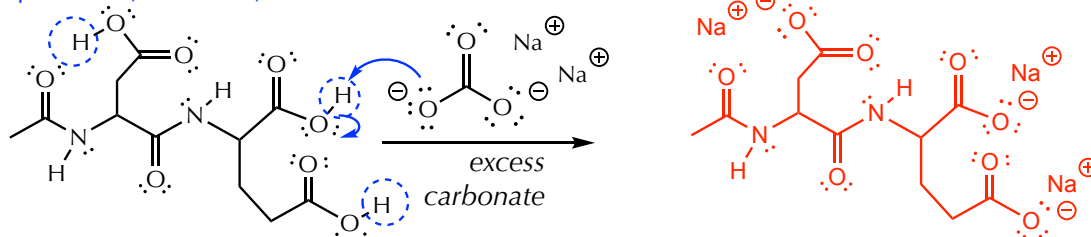
In CHEM 210 and 215, unless the guideline is given, the assumed default for this equilibrium constant is 10^3 . Thus, when the Brønsted acid product's pK_a value is $\geq +3$ pK_a units than the starting acid, the K_{EQ} is estimated to be greater than or equal to 10^3 . The definition of "complete reaction" is arbitrary and a guideline needs to be specified.

This guideline is required to answer this question. If carbonate is the Brønsted base, and it is in excess, then you can anticipate what the pK_a value range for a Brønsted acid needs to be to get this $\geq 10^3$ K_{EQ} .

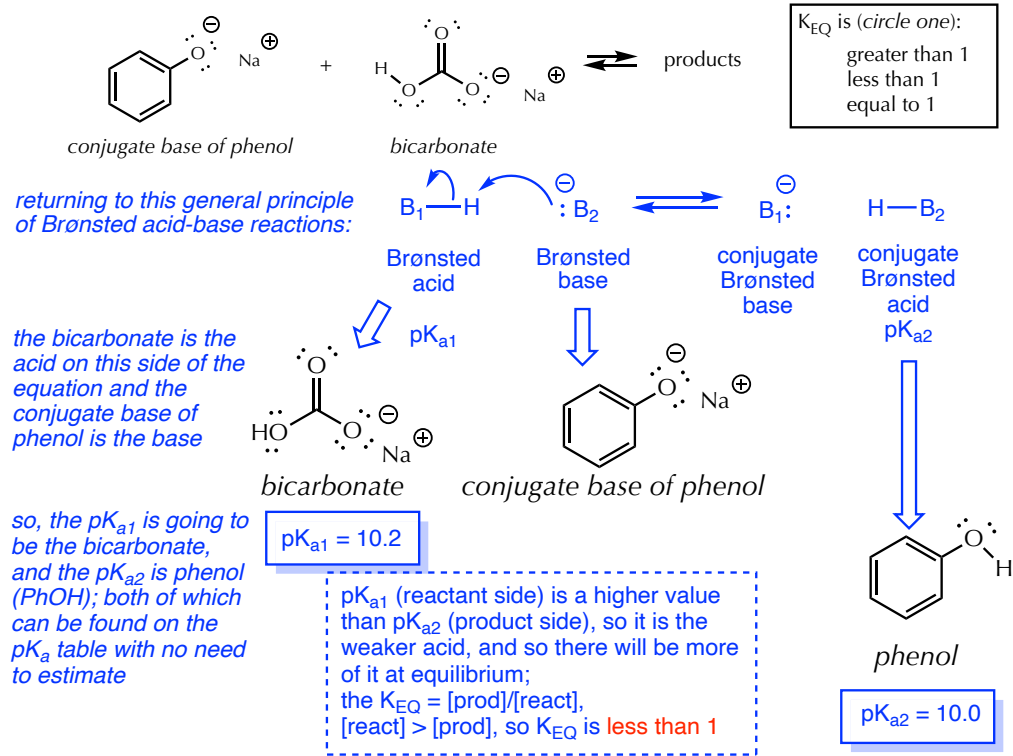


To answer this question, I need to know which of the potential Brønsted acids in **NAAG** have pK_a values ≤ 7.2 , which is exactly the same analogy-making exercise from part a.

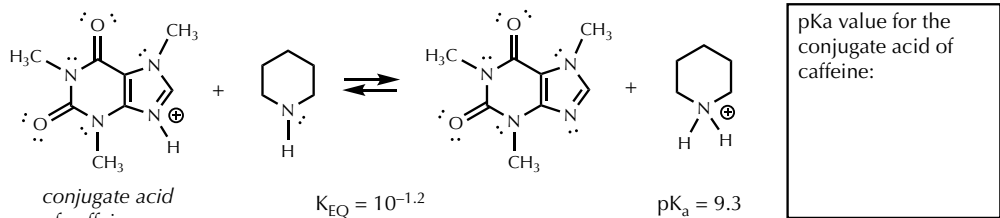
The C-H bonds are out of consideration, as they all have at least a pK_a of 19. The structural environment for the 3 O-H's are all identical to one another, and the 2 N-H's are also comparable, so two analogies are needed. The best analogy for the O-H's is the uncharged, sp^2 O attached to the C of a C=O, which is in turn attached to simple sp^3 hydrocarbons groups (pK_a 4.8 from the table). The N-H's have the same description, except they are N-H, and the best comparison is the pK_a 15.0 from the table. By the analysis above, carbonate (whose conjugate acid pK_a is 10.2) can be used to deprotonate anything with a pK_a of 7.2 or below with $K_{EQ} \geq 10^3$ - and so all three O-H's can be deprotonated, and will be, because excess carbonate is indicated.



3.36 It is possible to use pK_a values to assess an equilibrium constant. Is the value of the equilibrium constant for the 1:1 reaction between conjugate base of phenol and sodium bicarbonate greater than, less than, or equal to 1?

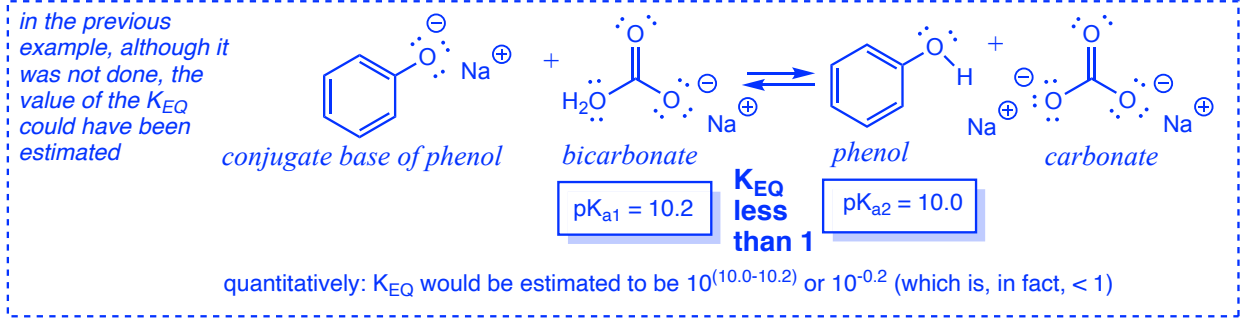


3.37 New pK_a values can be determined from measuring the equilibrium constant for an acid-base reaction that is carried out with a reaction partner whose pK_a value is known, and inferring what the pK_a value of the new compound must have been. Based on the following data, what is the estimated pK_a value for the conjugate acid of caffeine?

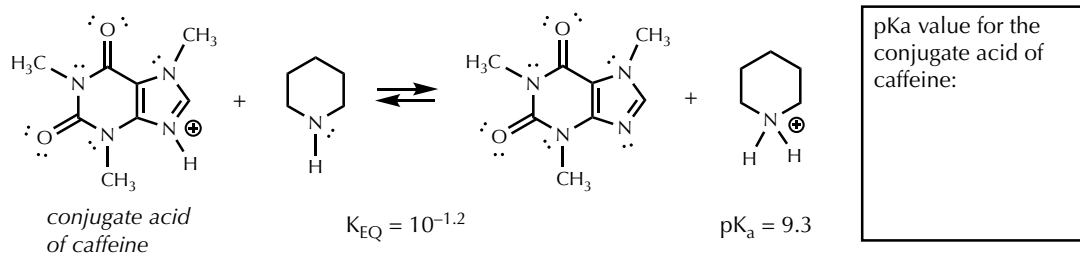


returning - again - to this general principle of Brønsted acid-base reactions, and taking account of the quantitative relationships:

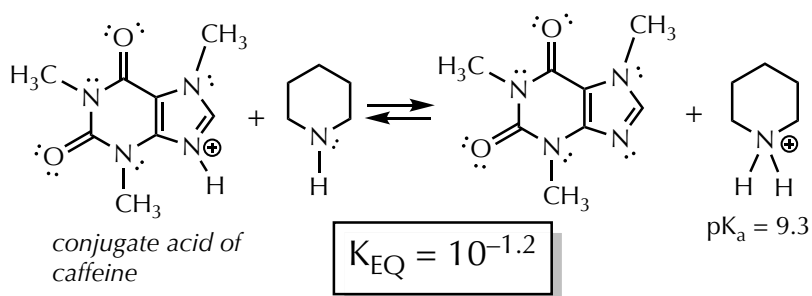
	B_1-H	$:B_2$	B_1^-	$H-B_2$	pK_{a1}	pK_{a2}	ΔpK_a	K_{EQ} (est.)
Brønsted acid				conjugate Brønsted acid	2	8	6	10^6
Brønsted base			conjugate Brønsted base		6	7	1	10^1
pK_{a1}				pK_{a2}	9	3	-6	10^{-6}
					8	8	0	$10^0 [=1]$
					5.5	3	-2.5	$10^{-2.5}$



3.37 New pK_a values can be determined from measuring the equilibrium constant for an acid-base reaction that is carried out with a reaction partner whose pK_a value is known, and inferring what the pK_a value of the new compound must have been. Based on the following data, what is the estimated pK_a value for the conjugate acid of caffeine?



in this reaction, the pK_a for the acid on the product side is given, and the K_{EQ} is given, and the question asks for the value of the pK_a of the acid on the left (the reactant side)



quantitatively: K_{EQ} is given as $10^{-1.2}$
 so it would be estimated to be $10^{(9.3 - pK_a \text{ reactant})}$
 therefore, pK_a of the reactant is **10.5**

this number needs to make sense:

- the K_{EQ} is $10^{-1.2}$ (a fraction, $[\text{prod}]/[\text{react}] < 1$), so the reaction lies to the left, $[\text{react}] > [\text{prod}]$
- the reaction lying to the left means that the reactant is less acidic (higher pK_a) than the product
- the difference in the values is 1.2, so the reactant's pK_a needs to be $9.3 + 1.2 = 10.5$