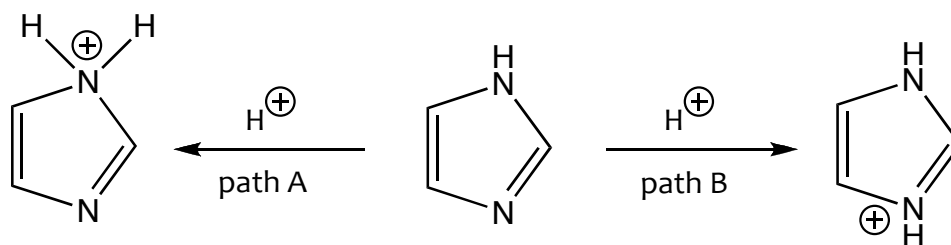
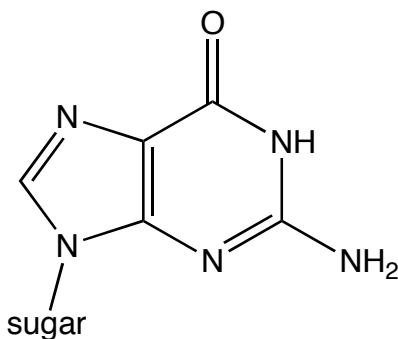


### Study Question 1: Acid-Base Concepts

1. For Table 1.2 in McMurry & Begley, draw the structure of the conjugate base produced by each acid. Which conjugate bases are stronger conjugate bases, the ones at the top or the bottom of the table?
2. For Table 1.3, which of the conjugate acids shown is the strongest, the one at the top of the table or the bottom?
3. One entry in these tables is imidazole, the ring system in the amino acid histidine, which is a major player at enzyme active sites. There are two nitrogens in imidazole. The scheme below shows each of them acting as a base. Which nitrogen is a better base? Explain your answer.



4. The DNA base guanine is shown below. Which heteroatom on guanine would be the most basic? Explain your choice.



5. If one looks in a biochemistry text book, there is always a chart of pKa's of amino acids (in Nelson & Cox, see Table 3-1 on pg 73). Some interesting trends in this data make good food for thought:

a. The pKa of the side of tyrosine is 10.07, but no value is given for the other alcohol-containing amino acids, serine and threonine. Why?

b. What would be an approximate value for the side chain pKa of serine? The side chain of cysteine is identical to that of serine except for the substitution of S for O. Why is the pKa of cysteine so much lower than serine?

c. The three amino acid side chains with a positive charge at physiological pH have rather different structures and pKa's, even though they all involve an N-H bond acting as an acid. Lysine serves as a good reference point, as it is a simple amine and is analogous to all simple amines whose conjugate acids have pKa's in the 9-12 range (lysine's is 10.53). The structural situation regarding histidine was covered in question #3 above; that of arginine is considered in problem 1.6 in the book which was assigned. Histidine's pKa is 6.00, arginine's is 12.48.

When acting as a base, what do the side chains of histidine and arginine have in common? Why then are their pKa's so different? Explain using structures or reactions.

6. Another interesting trend from these tables is that for the free amino acids, the pKa of the protonated  $\alpha$ -amino group is always within the typical range of 9-12. However, the pKa's of the  $\alpha$ -carboxylic acid groups are routinely lower than typical carboxylic acids. Even the two cases where the *side chains* have carboxylic acids are within the usual range. Explain why the  $\alpha$ -carboxylic acids have pKa's lower than typical whereas the protonated  $\alpha$ -amino groups are within the usual range. Write equations/reactions if it helps you understand what's going on (and it likely will).

7. Table 1.4 of McMurry & Begley gives the pKa's of some carbon acids (where it is the C-H bond that is dissociating).

a. Draw the conjugate base of each acid in this table. Ignoring the entry in brackets, what are these conjugate bases called as group – what is their functional group?

b. The dicarbonyl compounds all have lower pKa's than compounds with only one carbonyl group. Explain why using structures.

d. Write out the reaction of a ketone, thioester, ester and amide each acting as an acid at the  $\alpha$ -carbon. In this series, what is happening to the importance of resonance in the conjugate base? How do you know?

d. Explain why a ketone is more acidic than an ester.