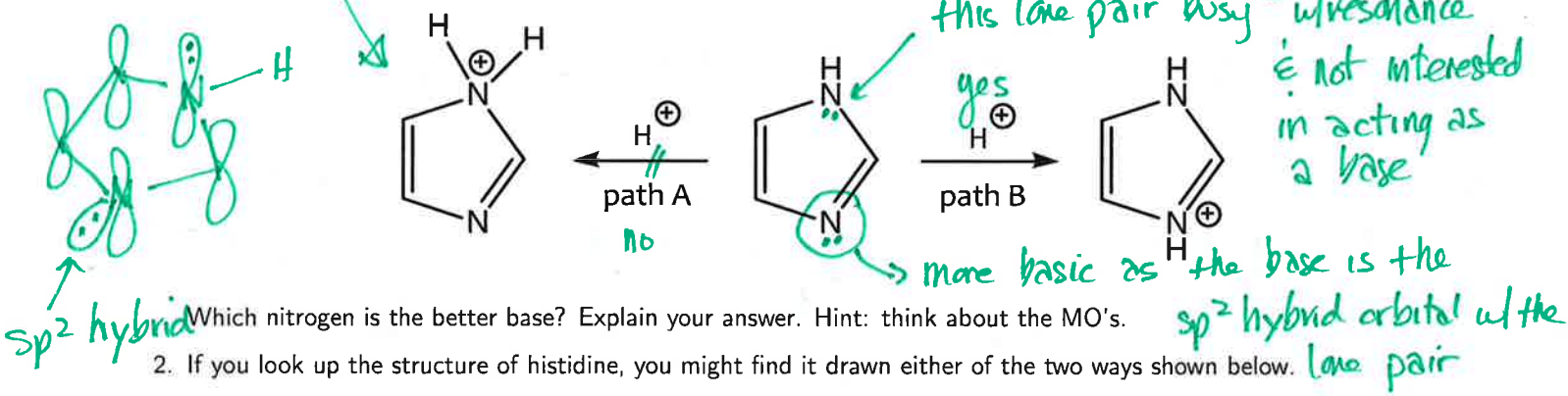
if this occurred, ya break up aromaticity w/ an sp^3 atom = no resonance = no aromaticity = bad idea

KEY

Study Question 1

If you are having trouble with drawing resonance forms, Karty section 1.11 has a very nice review.

1. Imidazole is the ring system in the side chain of the amino acid side chain. It's important to enzyme mechanisms because it is frequently present at active sites and has a pK_a of about 6, near physiological pH. There are two nitrogens in imidazole; the scheme below shows each nitrogen acting as a base.



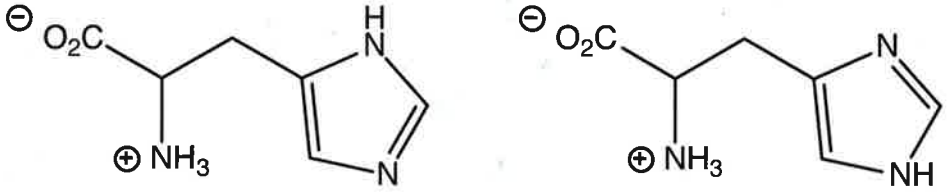
this lone pair "busy" w/ resonance & not interested in acting as a base

more basic as the base is the sp^2 hybrid orbital w/ the lone pair

sp^2 hybrid

Which nitrogen is the better base? Explain your answer. Hint: think about the MO's.

2. If you look up the structure of histidine, you might find it drawn either of the two ways shown below.



1,3-hydrogen shift called tautomerism

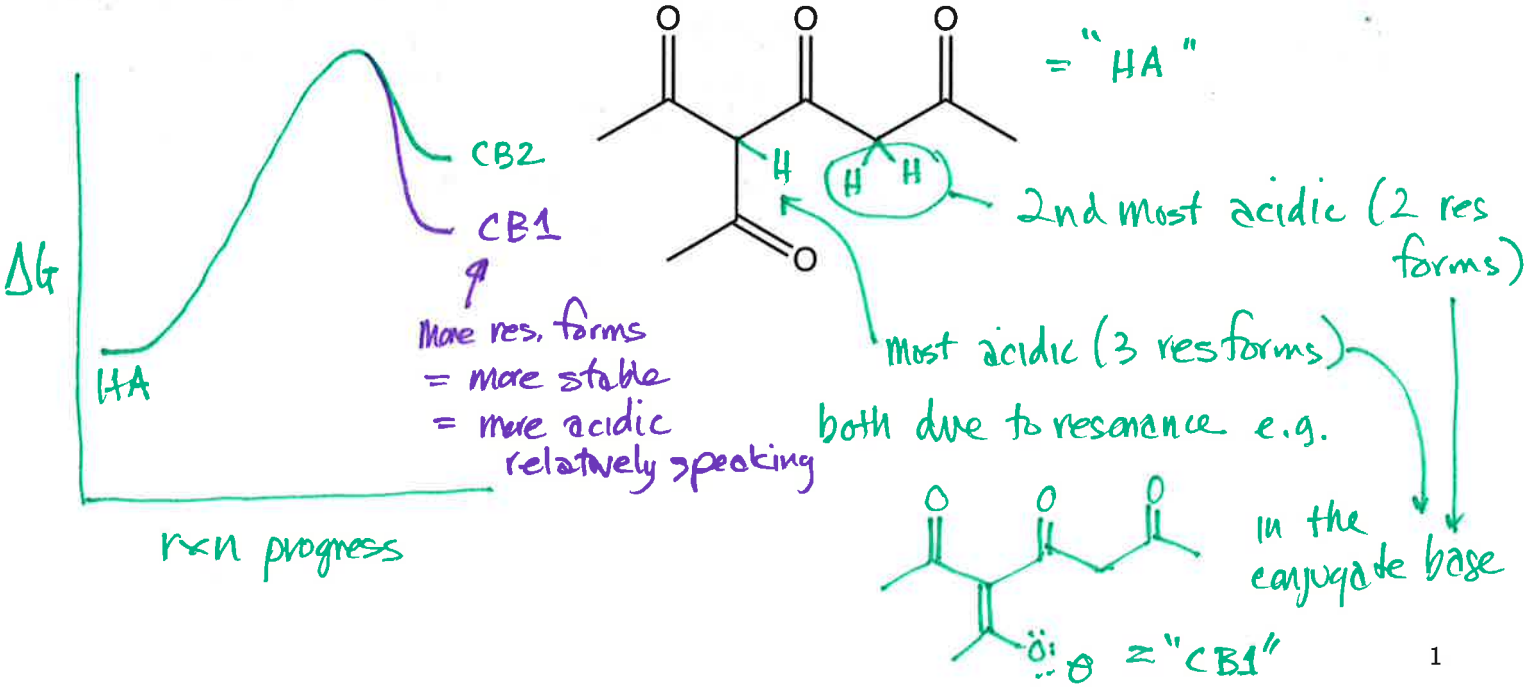
What is the difference between these two forms? Are they functionally different? What is the name of this phenomenon (hint: DOI: 10.1021/ja108943n)?

↳ they interconvert, so they are functionally the same

3. McBeg Table 2.4 has the pK_a's for the amino acids. There are some interesting trends in this data.
   (a) The pK_a for tyrosine is about 10, but no value is given for the other alcohols, serine and threonine. Why?
   (b) The pK_a of the α-carboxylates of free amino acids are typically about 2, but most carboxylates have a pK_a around 4-5. Explain why this is true. You probably should use a balanced equation or two, and ideally, an energy diagram.

PTO

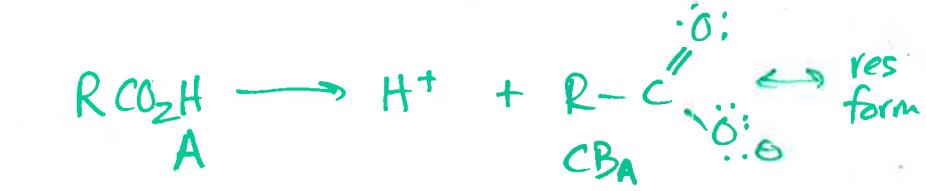
4. In the molecule below, which hydrogen is most acidic? Second-most acidic? Why? Explain with an energy diagram.



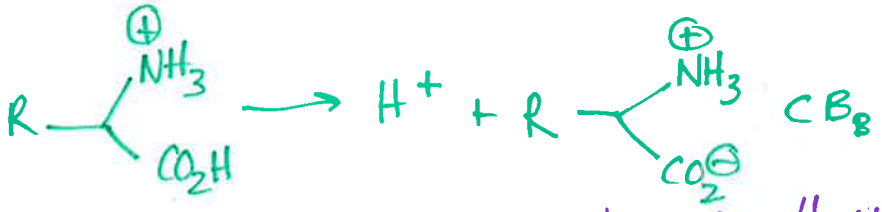
3a. Simple alcohols have pKa's in the 15-18 range which is too weak to dissociate in the physiologically relevant pH range, or even in water generally (at any pH)

3b.

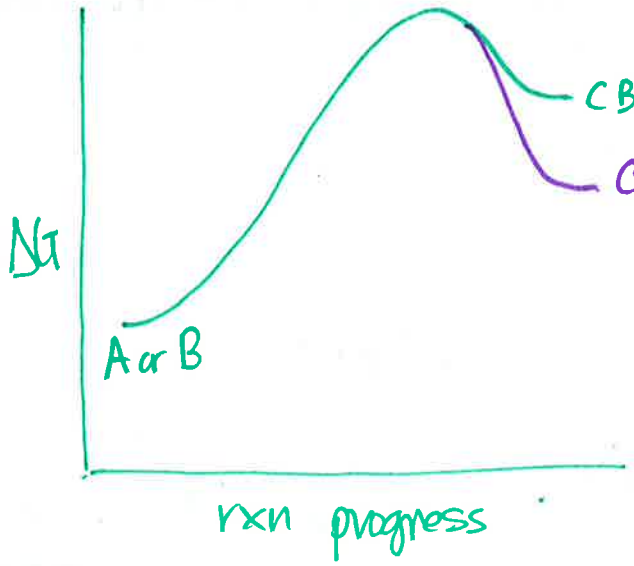
typical RCO_2H :



typical amino acid :



by either/both an inductive effect or an electrostatic effect, this conjugate base is more stable compared to the one above. Hence this 2nd rxn shifts to the right and has a lower pKa as a result.



this distance represents the increased acidity of B due to stabilization of its CB