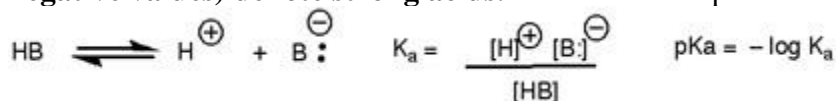


Five Key Factors That Influence Acidity

Acidity for different molecules and important factors that determine these values. Before we get started, however, let's quickly review the basics of acidity and basicity. Here's the condensed version:

1. **Bronsted acids are proton donors, Lewis acids are electron pair acceptors.** Converse: Bronsted base = proton acceptor, Lewis base = electron pair donor.
2. **A conjugate base is what you obtain when you remove a proton (H⁺) from a compound.** For instance, HO⁻ is the conjugate base of water. O²⁻ is the conjugate base of HO⁻. Conversely, conjugate acids are what you obtain when you add a proton to a compound. The conjugate acid of water is H₃O⁺.
3. Quick quiz: is pH 1 acidic or basic? **pKa is similar to pH in that low (and even negative values) denote strong acids.** That's because pKa is based on the equilibrium:



4. According to this, **anything which stabilizes the conjugate base will increase the acidity.** Therefore, pKa is also a measure of how stable the conjugate base is. Put another way, strong acids have weak conjugate bases, and vice versa.

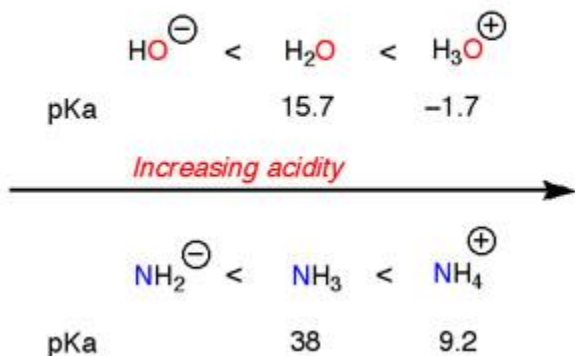
With that out of the way, let's get started.

Factor #1 – Charge.

Removal of a proton, H⁺, decreases the formal charge on an atom or molecule by one unit. This is, of course, easiest to do when an atom bears a charge of +1 in the first place, and becomes progressively more difficult as the overall charge becomes negative. The acidity trends reflect

this:

1. Acidity Increases with Increasing positive charge on an atom



Note that once a conjugate base (B⁻) is negative, a second deprotonation will make the dianion (B²⁻). While far from impossible, forming the dianion can be difficult due to the buildup of negative charge and the corresponding electronic repulsions that result.

Factor #2 – The Role of the Atom

This point causes a lot of confusion due to the presence of two seemingly conflicting trends.

Here's the first point: acidity increases as we go *across* a row in the periodic table. This makes sense, right? It makes sense that HF is more electronegative than H₂O, NH₃, and CH₄ due to the greater electronegativity of fluorine versus oxygen, nitrogen, and carbon. A fluorine bearing a negative charge is a happy fluorine.

But here's the seemingly strange thing. HF itself is not a "strong" acid, at least not in the sense that it ionizes completely in water. HF is a weaker acid than HCl, HBr, and HI. What's going on here?

2. Across the periodic table, acidity increases with electronegativity...

	CH ₄	<	NH ₃	<	H ₂ O	<	HF
pKa	~50		38		15.7		3.2
Electronegativity	2.5		3.0		3.4		4.0

...but down the periodic table, acidity increases with size.

	HF	<	HCl	<	HBr	<	HI
pKa	3.2		-8.0		-9.0		-10
Electronegativity	4.0		3.0		2.8		2.5
Ionic radius (picometres)	133		181		196		220

Also holds for oxygen versus sulfur...

	H ₂ O	<	H ₂ S
pKa	15.7		7.0
	H ₃ COH	<	H ₃ CSH
pKa	15.5		10

You could make two arguments for why this is. The first reason has to do with the shorter (and stronger) H-F bond as compared to the larger hydrogen halides. The second has to do with the *stability of the conjugate base*. The fluoride anion, F(-) is a tiny and vicious little beast, with the smallest ionic radius of any other ion bearing a single negative charge. Its charge is therefore spread over a smaller volume than those of the larger halides, which is energetically unfavorable: for one thing, F(-) begs for solvation, which will lead to a lower entropy term in the ΔG .

Note that this trend also holds for H₂O and H₂S, with H₂S being about 10 million times more acidic.

Factor #3 – Resonance.

A huge stabilizing factor for a conjugate base is if the negative charge can be delocalized through resonance. The classic examples are with phenol (C₆H₅OH) which is about a million times more acidic than water, and with acetic acid (pKa of ~5).

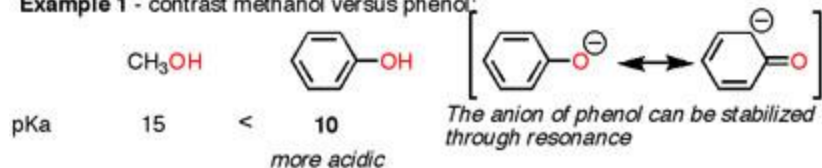
3. Resonance

Remember, **any structural feature that increases the stability of the conjugate base will increase acidity.**

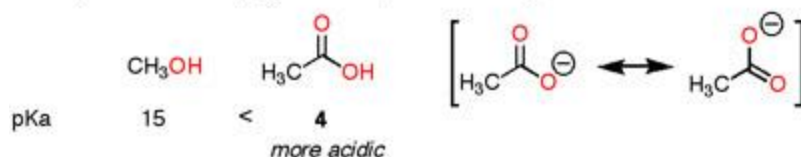
Key question: can the lone pair of the conjugate base participate in resonance with an adjacent π bond?

Resonance will increase the stability of the conjugate base (therefore increasing acidity) because the negative charge can be delocalized.

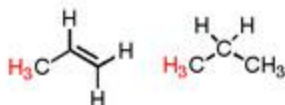
Example 1 - contrast methanol versus phenol:



Example 2 - alcohols (e.g. methanol) versus carboxylic acids



Question: Which proton (in red) would you expect to be more acidic?



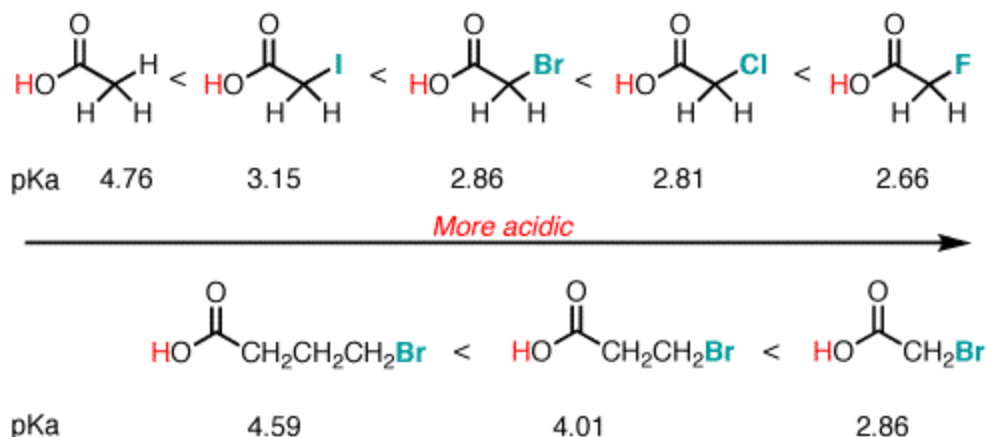
Watch out though – it isn't enough for a π system to simply be adjacent to a proton – the electrons of the conjugate base have to be in an orbital which allows for effective overlap (for a dastardly trick question in this vein that routinely stymies Harvard premeds, look [here](#).)

Factor #4 – Inductive effects. Electronegative atoms can draw negative charge toward themselves, which can lead to considerable stabilization of conjugate bases. Check out these examples:

4. Electronegativity and inductive effects:

Two principles - electron-withdrawing substituents can increase acidity of a nearby atom, which **increases with electronegativity** and **decreases with increasing distance to the atom**.

Electronegativity increases in the order $F > Cl > Br > I$:

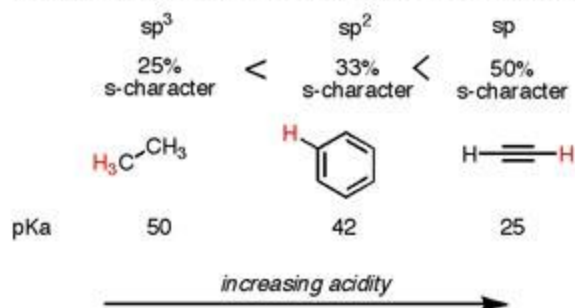


Predictably, this effect is going to be related to two major factors: 1) the electronegativity of the element (the more electronegative, the more acidic) and the distance between the electronegative element and the negative charge.

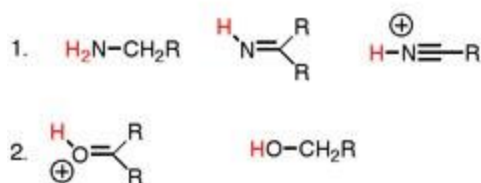
Factor #5 – Orbitals. Again, the acidity relates nicely to the stability of the conjugate base. And the stability of the conjugate base depends on how well it can accommodate its newfound pair of electrons. In an effect akin to electronegativity, the more s character in the orbital, the closer the electrons will be to the nucleus, and the lower in energy (= stable!) they will be.

5. Orbitals

The higher the *s*-character of a bond to hydrogen, the more acidic it will be.



Questions: What do you think about the acidity of the following protons in red?



Look at the difference between the pKa of acetylene and alkanes – 25! That's 10 to the power of 25, as in, "100 times bigger than Avogadro's number". Just to give you an idea of scale. That's the amazing thing about chemistry – the sheer *range* in the power of different phenomena is awe-inspiring.

There's actually a mnemonic to help you remember these effects.

Charge

Atom

Resonance

Dipole Induction

Orbitals

= **CARDIO**.

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