Introductory Organic Chemistry II
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Module 06
Lecture 40
Active Methylene Group

So, in this lecture, we look at the concept of Active Methylene Group. We have already seen some glimpses of this in some of the previous lectures. But now we will try and understand this concept a little better in terms of acidity, and pKa, and so on. So, the first concept that we need to understand is acidity.

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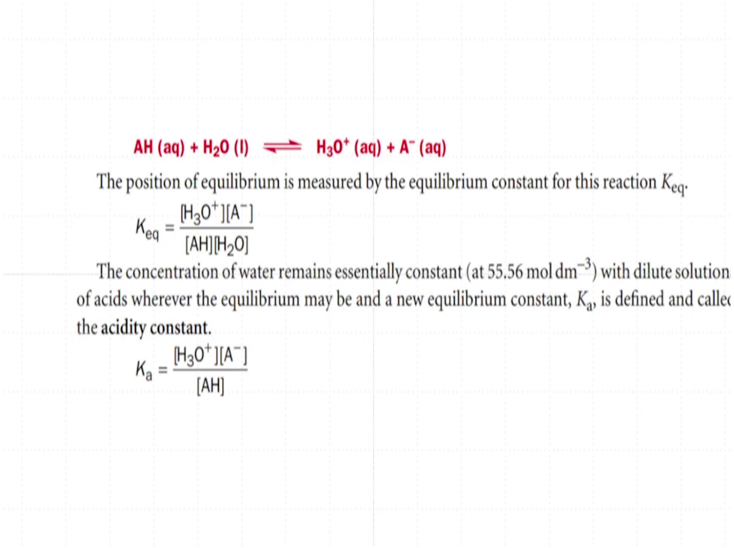

$AH\ (aq) + H_2O\ (l) \rightleftharpoons H_3O^+\ (aq) + A^-\ (aq)$

The position of equilibrium is measured by the equilibrium constant for this reaction K_{eq}.

$$K_{eq} = \frac{[H_3O^+][A^-]}{[AH][H_2O]}$$

The concentration of water remains essentially constant (at 55.56 mol dm^{-3}) with dilute solution of acids wherever the equilibrium may be and a new equilibrium constant, K_a, is defined and calle the **acidity constant.**

$$K_a = \frac{[H_3O^+][A^-]}{[AH]}$$

So, if we take an acid AH, and put it in water, then if it is an acid, then it is going to equilibrate to produce H_3O^+ and A^-. And the important concept here is that the position of this equilibrium is dictated by the stability of the conjugate base, which is A^-.

So now, the way we would experimentally determine the stability is to measure the equilibrium constant, and the equilibrium constant is nothing but the concentration of H_3O^+, multiplied by the concentration of the conjugate base, divided by the concentration of the acid and water.

Now, it is really important that we understand this, because you know the conjugate base stability is the primary or the most important factor for determining the strength of an acid. Now, what we know from our mini discussions previously in other courses as well, is that the water concentration here is so large, it is 55.56 molar, and you know in very dilute solutions, this concentration is not going to change. So therefore, this concentration of water is more or less a constant.

And so, we define a new constant, which is known as the acidity constant Ka, which is nothing but the concentration of H_3O^+ multiplied by concentration of A^- divided by the concentration of the acid. So, if you see here, the stronger the acid is, the more stable the conjugate base, the concentration of A^- is going to go up.

So, the equilibrium will be more towards the right. So higher the Ka value, the better the acid is. Now, the problem or the situation is that we are going to be dealing with numbers such as 10^{-3}, 10^{-4}, 10^{2}, 10^{3}, or things like that. So, that is not very easy or very convenient for us to compare.

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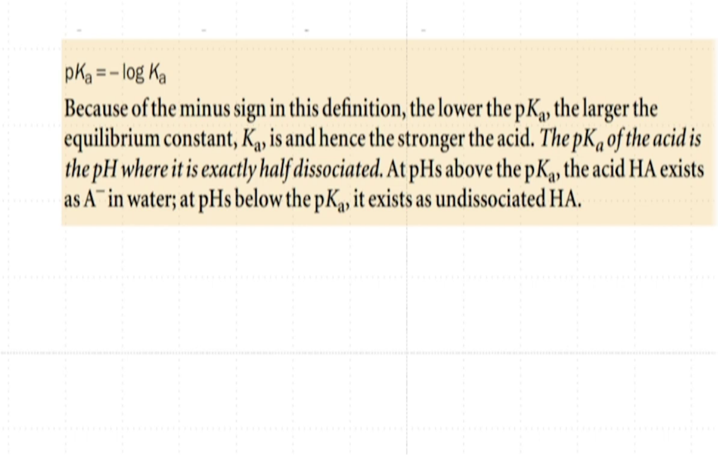
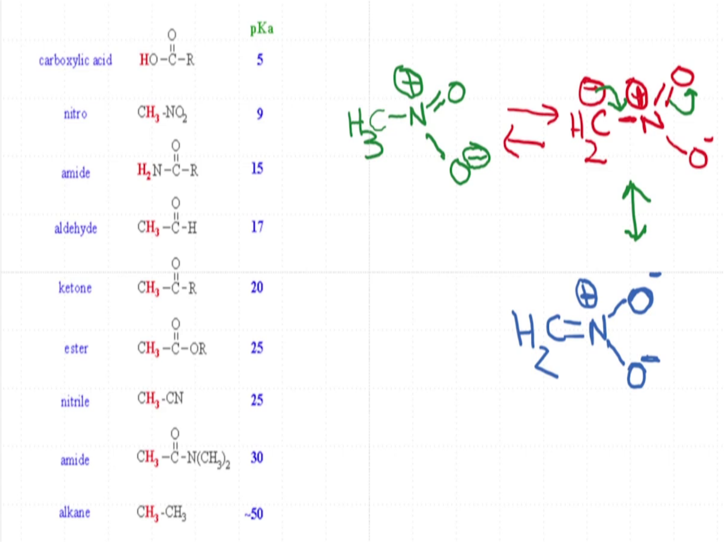
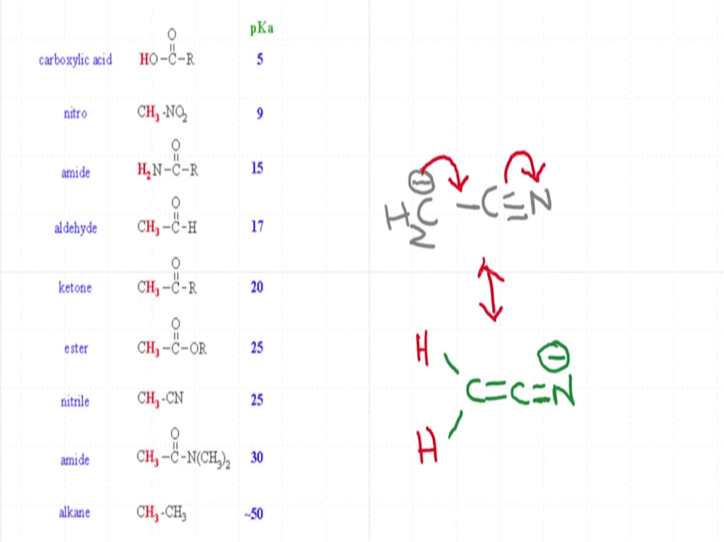


$pK_a = -\log K_a$

Because of the minus sign in this definition, the lower the pK_a, the larger the equilibrium constant, K_a, is and hence the stronger the acid. *The pK_a of the acid is the pH where it is exactly half dissociated.* At pHs above the pK_a, the acid HA exists as A^- in water; at pHs below the pK_a, it exists as undissociated HA.



		pKa
carboxylic acid	$HO-\overset{O}{\overset{\|}{C}}-R$	5
nitro	CH_3-NO_2	9
amide	$H_2N-\overset{O}{\overset{\|}{C}}-R$	15
aldehyde	$CH_3-\overset{O}{\overset{\|}{C}}-H$	17
ketone	$CH_3-\overset{O}{\overset{\|}{C}}-R$	20
ester	$CH_3-\overset{O}{\overset{\|}{C}}-OR$	25
nitrile	CH_3-CN	25
amide	$CH_3-\overset{O}{\overset{\|}{C}}-N(CH_3)_2$	30
alkane	CH_3-CH_3	~50



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So, the other parameter is used, which is nothing but pKa. pKa is defined as the negative log of the Ka. And because this minus sign is there, in this definition the larger the equilibrium constant Ka the better the acid is, that is what we learned. But it inversely sort of correlates with pKa. So, the smaller the value of pKa the better the acid is.

So again, this is a sort of a refresher of what we have done in the past. Now with this background, let us look at some table of pKa. So, here we start from the bottom. So, here is the pKa of an alkane is really small, it is not measurable even. The Ka value is 10^{-50}, and the pKa is about 50. Now, as we go up this table, we find that the pKa values are becoming lower.

And so, the benchmark value that we try to look for is the carboxylic acid, which is around 5. Now, let us look at the next molecule here, which is Nitromethane. So, nitromethane, whose structure I have drawn here, has a nitro group attached to a CH_3. And this as you know, there is a strongly electron withdrawing group. So, if it undergoes deprotonation, that is it is in equilibrium with its anion. Now the anion one can draw resonance form where all the participating atoms have an octet.

And so, this is a fairly stable resonance form and therefore, one can suggest that the conjugate base is quite stable. So therefore, nitromethane being a strong acid is actually quite understandable. If we go down this table, I think we have already looked at amides, aldehydes, and ketones, and esters. The next molecule that we are going to look at is the Nitrile. So, nitrile is our cyano compound, is a very interesting molecule.

So, the carbon here is sp hybridized, and the nitrogen is also sp hybridized. And so, there is a triple bond over here. Now, once the nitrile undergoes deprotonation, it forms this anion. And this anion again, one can draw resonance form where this negative charge is delocalized across these three atoms.

Now, this makes the molecule certainly more acidic than methane. So, if you compare it with methane, it is certainly more acidic. But this conjugation, and the resulting stability is not as high as what you would achieve with let us say, a ketone. So therefore, there is still a difference between a nitrile and a ketone, and the ketone being more acidic.

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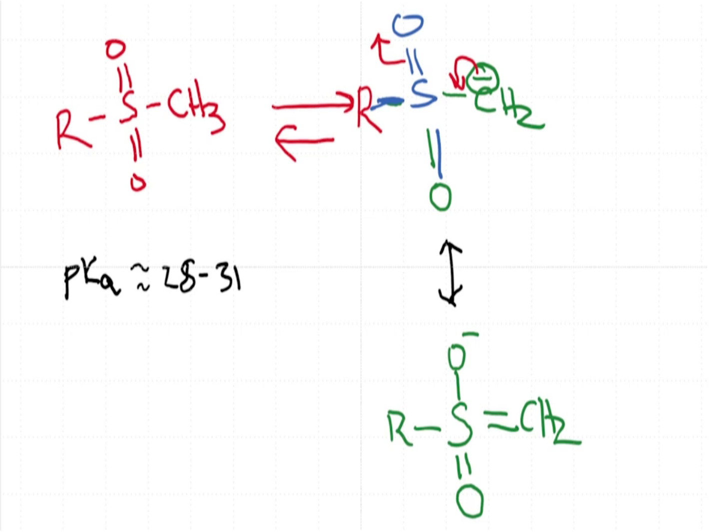

The next compound that we look at is not present normally in these pKa tables, but it is an important compound nevertheless, which is a sulfone. So, sulfones are also acidic, and they can be deprotonated, the pKa values are somewhere between 28 and 31. And so once you deprotonate it, you get the CH_2^-, and then the CH_2^- can delocalize and produce this kind of anion.

So here, if you notice the negative charges is on an electronegative atom, which is oxygen, so therefore this can also be an acidic, that is, sulfones can also be acidic. One comment here is that the sulphur, you know, the hybridization here and I mean, it is lower in the periodic table so, the overlap here is not very good.

So, if I compare this with a carboxylate, or something similar to that the overlap between the orbitals is not as good. And so, the stability afforded by that correspondingly is not very high, and therefore the pKa value is substantially higher than what we would expect with a ketone.

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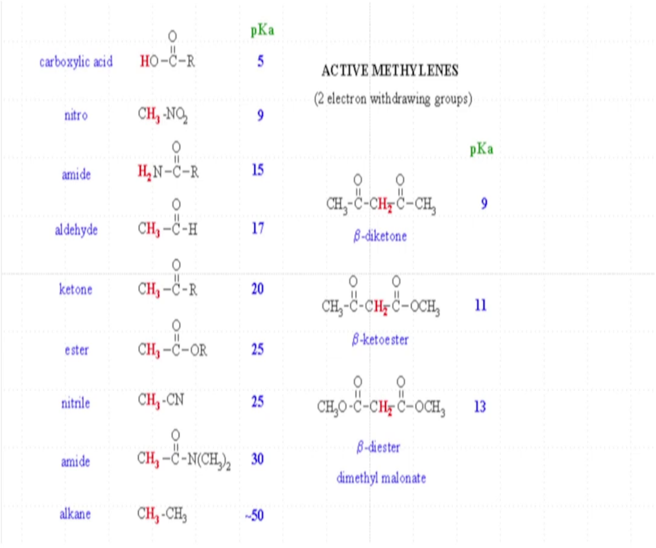

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amide	$CH_3-\overset{\overset{O}{\|}}{C}-N(CH_3)_2$	30
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ACTIVE METHYLENES

(2 electron withdrawing groups)

	pKa
$CH_3-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-CH_3$ β-diketone	9
$CH_3-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-OCH_3$ β-ketoester	11
$CH_3O-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-OCH_3$ β-diester dimethyl malonate	13

So, with that, now, let us look at the concept of active methylene. So, active methylene is usually referred to when you have the ability to have very strong electron withdrawing groups on a particular methylene carbon. So, this is we were discussing about methyl. Now, here is a methylene group, which is an active methylene group.

So, if you see here, this is a diketone, and the pKa value is about 9. So, if I take a mono-ketone that is just a simple ketone, the value is around 20. So, there is a substantial lowering of pKa values and increasing in acidity. And as you can see here in this table, there are a couple of other examples where you have a keto-ester and a diester. These are things that we will look at in more detail shortly.

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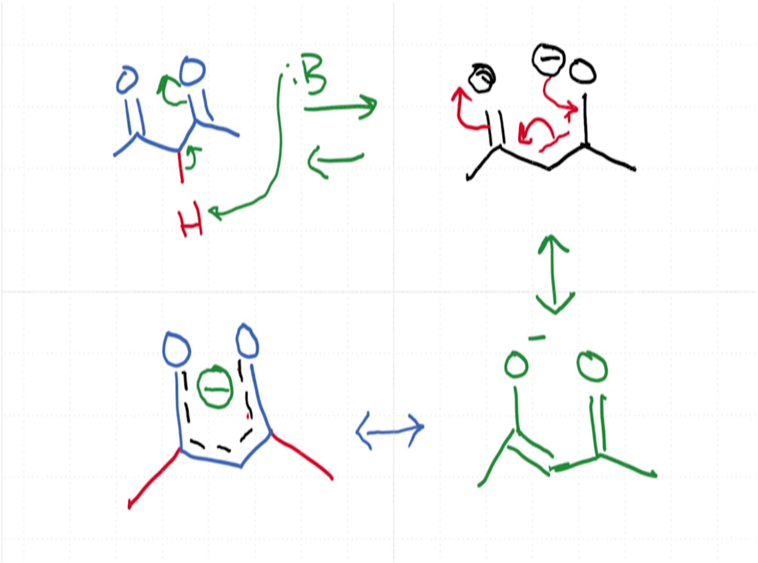

So, one of the ways in which we understand the extremely good acidic properties of these active methylene compounds is because if you do a deprotonation on this, you get this enolate. And once you get the enolate, the enolate can nicely delocalize and produce another resonance form as shown here.

And so, in essence, it is a resonance hybrid that we are going to deal with which is nicely delocalized across 5 atoms. So, with this, you can sort of understand why these compounds which are known as active methylene groups are quite acidic and how we can use them later. We will discuss later about how you can use them to exploit in synthetic chemistry.