Organic Chemistry-2

Semester-2, CBCS

Course: CEMA CC-2-3-TH

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Recommended texts:

The Concept of Acidity and Basicity in Organic Chemistry

Effect of structure on acid and base strength of organic molecules:

C] Resonance Effect:

Recall from our previous discussions that if the conjugate base $X^-$ of any acid HX has a lower tendency to regain a proton compared to another conjugate base $Y^-$ of another acid HY, then, between $X^-$ and $Y^-$, the former is a weaker base.

Consequently, from Brønsted-Lowry theory, we can also safely predict HX to be a stronger acid than HY.

But, how do we know that between $X^-$ and $Y^-$, which one has a lower tendency to regain a proton?

Applying our common sense, we can consider the extent of the dispersion of electron density over the conjugate bases - higher the dispersion of the negative charge density in the conjugate base, lower is its tendency to regain the proton, weaker is that conjugate base, and thus, higher is the acidity of the corresponding acid.

Similarly, basicity order is explained by considering the electron pair donation capacity of the base in question - if the lone pair is donated easily, the basicity of the base is higher than any other base which is relatively unwilling to give away its electron pair.

One major factor that is responsible for the dispersion of electron density is the resonance effect.

Let us consider the following order of acidity:

\[
\begin{array}{ccc}
 R-\text{OH} & & R-\text{COOH} \\
pK_a & ca. 18 & 9.95 & ca. 4-5 \\
\end{array}
\]

To estimate the relative stability of the corresponding conjugate bases in terms of charge dispersion we have to remember the following:

Greater the dispersion of charge in a conjugate base, the more stable that anion (conjugate base) is, lower is its tendency for proton capture, and lower is the basicity.

...all of these can only mean that...

... the corresponding acid is a stronger acid, compared to any other acid whose conjugate base, because of a less efficient charge dispersal mechanism, is more willing to grab a proton.
The Concept of Acidity and Basicity in Organic Chemistry

Effect of structure on acid and base strength of organic molecules:

C] Resonance Effect:

\[
\begin{align*}
\text{pK}_a & \quad \text{R-OH} & \quad \text{Ph-OH} & \quad \text{R-COOH} \\
\text{ca. 18} & \quad 9.95 & \quad \text{ca. 4-5} \\
\text{acidity increases} & \quad & \quad & \\
\end{align*}
\]

The conjugate base from ROH is RO\(^{-}\) where we have no extra stabilization. R-O\(^{-}\) (no resonance stabilisation)

The conjugate base from phenol is PhO\(^{-}\) which is stabilized through resonance with the participation of benzene nucleus. The canonical forms are:

Again, phenol itself is also resonance-stabilized:

We note that there is a charge separation in case of phenol which is absent in case of phenoxide. So resonance stabilization of phenoxide ion is more efficient than that of phenol.

But that does not mean that phenoxide is overall more stable than phenol, no. That cannot be the case because the pK\(_a\) value is close to 10, implying \(K_a \sim 10^{-10}\), meaning that in the acid base equilibrium with water as the base, only a very small fraction of the total number of phenol molecules is ionised.

The only point we are trying to make is that in phenoxide resonance is more efficient than it is in phenol.

The conjugate base of carboxylic acid is RCOO\(^{-}\), which is stabilized through resonance, the canonical forms are:

However, carboxylic acid itself is resonance-stabilized:

Again there is a separation of charge. So resonance stabilization of carboxylate anion is higher than that of carboxylic acid. Again, this is not to say that the carboxylate anion is thermodynamically more stable than the carboxylate itself; just that the resonance in the ion is more effective than in the acid.
The Concept of Acidity and Basicity in Organic Chemistry

Effect of structure on acid and base strength of organic molecules:

C] Resonance Effect:

\[
\begin{align*}
\text{pK}_a & \quad \text{ca. 18} & 9.95 & \quad \text{ca. 4-5} \\
\text{acidity increases}
\end{align*}
\]

We have understood that the phenoxide ion is more stable than the alkoxide ion by virtue of resonance stabilisation of the former.

So what about the phenoxide and the carboxylate? It turns out that the carboxylate anion is comparatively more stable than the phenoxide. Consider the following reasons:

1) For carboxylate anion, the two resonance canonicals are equivalent. This implies greater resonance stability for the carboxylate, but this is not the case with phenoxide where the canonicals are not equivalent.

2) For carboxylate anion, each canonical form places the negative charge on the more electronegative element oxygen, whereas for phenoxide anion we have three canonical forms where the less electronegative carbon bears the negative charge. In addition, aromaticity is lost in the ring in delocalising the negative charge.

3) In case of carboxylate ion, there is also a strong inductive withdrawal effect of the carbonyl carbon adjacent to the oxyanion centre, but in case of phenoxide this type of -I effect of neighboring sp2 hybridized ring carbon is not so effective.

Of course, this last factor has nothing to do with resonance, but it certainly helps in delocalizing the excess electron density on the oxygen atoms. Also compare the situation of the alkoxide where the carbon adjacent to the oxyanion centre is, in fact, less electronegative an sp3 hybridized.

Thus we have the following order of stability of conjugate bases:

\[
\begin{align*}
\text{R-O}^- & \quad \text{stability increases} & \text{R-O}^- & \quad \text{sp2} & \quad \text{sp3} \\
\end{align*}
\]

Recall that \( \chi_{C(sp2)} > \chi_{C(sp3)} \)

Thus, the EW capacity of sp2 carbon is greater than that of sp3 carbon.
The Concept of Acidity and Basicity in Organic Chemistry

Effect of structure on acid and base strength of organic molecules:

C] Resonance Effect:

\[ \text{R-OH} \quad \text{Ph-OH} \quad \text{R-COOH} \]

\[ pK_a \quad \text{ca. 18} \quad 9.95 \quad \text{ca. 4-5} \]

acidity increases

We have established the following order of stability of conjugate bases:

\[ \text{R-O}^- \quad \text{Ph-O}^- \quad \text{R-COO}^- \]

stability increases

So on moving from left to right in this series, the corresponding acids have a higher tendency to release the proton and thereby the respective acid-base eqm. involving water as the base common to all three, will shift more towards right.

However, none of those equilibrium will be favoured towards the RHS, the pKa values tell us so. It is just that for the carboxylic acid the extent of dissociation of the acid molecule will be greater than it will be for the phenol, and even less so for the alcohol.

Thus we have the given order of acidity.

This acidity order is exploited in separating a mixture of a carboxylic acid and phenolic compound, none of which are water soluble.

Due to its higher acidity, the carboxylic acid protonates the bicarbonate to afford carbonic acid which, in turn, is decomposed to CO₂ and water. The resulting carboxylate anion is soluble in the aqueous solution of bicarbonate. However, phenols are less acidic and cannot protonate the bicarbonate ion efficiently and remain insoluble in an aqueous solution of sodium bicarbonate.
The Concept of Acidity and Basicity in Organic Chemistry

Effect of structure on acid and base strength of organic molecules:

C) Resonance Effect:

\[
\begin{align*}
\text{R-OH} & \quad \text{phenol} \\
\text{R-COOH} & \quad \text{benzoic acid}
\end{align*}
\]

\[pK_a = \begin{align*}
\text{ca. 18} & \quad \text{(phenol)} \\
\text{ca. 4-5} & \quad \text{(benzoic acid)}
\end{align*}\]

This acidity order is exploited in separating a mixture of a carboxylic acid and phenolic compound, none of which are water soluble.

Due to its higher acidity, the carboxylic acid protonates the bicarbonate to afford carbonic acid which, in turn, is decomposed to CO\(_2\) and water. The resulting carboxylate anion is soluble in the aqueous solution of bicarbonate. However, phenols are less acidic and cannot protonate the bicarbonate ion efficiently and remain insoluble in an aqueous solution of sodium bicarbonate.

Using this differential solubility in aqueous bicarbonate solution, a mixture of benzoic acid and \(\beta\)-naphthol might be separated following the technique outlined below:

\[
\begin{align*}
\text{phenol} & \quad \text{benzoic acid} \\
\text{\(pK_a\) 9.98} & \quad \text{\(pK_a\) 4-5}
\end{align*}
\]

\[
\text{(water soluble)}
\]

\[
\begin{align*}
\text{H}_2\text{O} & + \text{CO}_2 \\
\text{effervescence}
\end{align*}
\]

You have learnt of this sort of solubility-based separation of binary solid mixtures in your first semester practical.
The Concept of Acidity and Basicity in Organic Chemistry

Effect of structure on acid and base strength of organic molecules:

C) Resonance Effect:

As we go on increasing the number of electron-withdrawing groups in the acid, the acidity of the same increases. A case in point is the following series:

\[
\begin{align*}
\text{pK}_a & \quad \text{OH} \quad \text{OH} \quad \text{OH} \quad \text{OH} \\
9.95 & \quad 8.4 & \quad 7.1 & \quad 0.3 \\
\text{苯} & \quad \text{苯} & \quad \text{苯} & \quad \text{苯} \\
\end{align*}
\]

This order can be explained by judging the proton capture tendency of the respective conjugate bases:

1. Phenoxide ion, conjugate base of phenol.
   Here the negative charge over phenoxyde ion is dispersed through resonance with the participation of benzene nucleus.

2. Conjugate base of \text{m-nitrophenol}.
   Here the negative charge over phenoxyde ion is dispersed through resonance with the participation of benzene nucleus. The -I effect of nitro group aids to disperse the negative charge over the phenoxyde ion. Thus the negative charge dispersal here is higher than that seen in simple phenoxyde ion. But NO₂ cannot accommodate the negative charge here through its -R effect.

3. Conjugate base of \text{p-nitrophenol}.
   Here the negative charge over phenoxyde ion is dispersed through resonance with the participation of benzene nucleus. Both the -I and the -R effect of nitro group aid to disperse the negative charge over the phenoxyde ion. Thus here the dispersion of negative charge is higher than that seen in the case of \text{m-nitrophenol}.

4. Conjugate base of picric acid.
   Here the negative charge over phenoxyde ion is dispersed through resonance with the participation of benzene nucleus. The -I and the -R effect of all three nitro groups at \text{ortho-} and \text{para-} positions aid to disperse the negative charge over the phenoxyde ion. Thus here the dispersion of negative charge is greatest among all the conjugate bases and it has the lowest tendency to capture a proton.
The Concept of Acidity and Basicity in Organic Chemistry

Effect of structure on acid and base strength of organic molecules:

C] Resonance Effect:

The resonance effect is also responsible for the higher acidity of \( p \)-chlorophenol compared to \( p \)-fluorophenol, although a reverse order is expected from a consideration of inductive electron-withdrawal. Recall that F is more electronegative than Cl, so F has a greater inductive EW effect than Cl.

Let us consider the conjugate bases:

In conjugate base from \( p \)-chlorophenol negative charge is dispersed through resonance with the participation of benzene nucleus and low-lying vacant d-orbitals of chlorine at the \textit{para} position.

In addition, the halogen atom may impart its ++R effect which intensifies the negative charge over the benzene nucleus and acts as an acid-weakening influence. This ++R effect is expected to be more pronounced with fluorine because of the proper matching of the involved orbitals (2p of C and 2p of F).

Halogen atoms also exhibit -I effect, but it is less important here because of the larger distance between the halogen and the oxygen atom carrying most of the negative charge.

Thus, from the above analysis we can conclude that \( p \)-chlorophenoxide anion is expected to have a lower tendency to regain the proton than the \( p \)-fluorophenoxide anion. Thus \( p \)-chlorophenol is more acidic than \( p \)-fluorophenol.
The Concept of Acidity and Basicity in Organic Chemistry

Effect of structure on acid and base strength of organic molecules:

C] Resonance Effect:

When the acidic proton is attached to a carbon atom, the acid is called a carbon acid. Usually hydrocarbons are very weak acids, because carbon itself is not at all equipped to handle a negative charge upon it. But if the electron density from the carbon atom can be efficiently dispersed, we can expect a dramatic enhancement of carbon acids’ acidity.

This is what happens when we attach with that carbon groups which can impart strong resonance electron withdrawing (-R) effect, as the conjugate base then gains stability by dispersion of electron density.

For example, while alkanes have typical pK\(_a\) values in the range of 45-50, just the presence of one carbonyl group directly adjacent to a C-H bond drops the pK\(_a\) to approximately 20 - a rise of 10\(^{25}\) to 10\(^{30}\) fold in acidity from an alkane.

In the conjugate base of an alkane the negative charge must reside on a carbon, whereas with a ketone, the negative charge of the conjugate base (also known as the enolate ion) is dispersed through resonance in which the more contributing canonical form has the negative charge on the more electronegative oxygen atom.

The carbonyl carbon also exerts a strong -I effect which further helps in stabilizing the enolate ion. Thus this conjugate base of the ketone has a much lower tendency to regain the proton than the conjugate base of an alkane. It follows that the ketone is much more acidic than the alkane, as we can see in the pK\(_a\) values.

\[
\begin{align*}
\text{H}_3\text{C}-\text{CH}_3 & \quad \text{H}_2\text{C}-\text{CH}_3 \\
\text{pK}_a \text{ ca. 50} & \quad \text{pK}_a 20
\end{align*}
\]

The effect of different electron-withdrawing groups on the pK\(_a\) value is demonstrated amply in the following table:

<table>
<thead>
<tr>
<th>Effect of Z on pK(_a) of H(_2)H(_3)C-CZ</th>
<th>Z</th>
<th>-H</th>
<th>-C=O</th>
<th>-C≡N</th>
<th>-COEt</th>
<th>-CO</th>
<th>-NMe(_2)</th>
<th>-NO(_2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pK(_a)</td>
<td>50</td>
<td>20</td>
<td>25</td>
<td>23</td>
<td>30</td>
<td>10.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Clearly, the greater the electron-withdrawing power of Z is, greater is the acidity of MeCH\(_2\)Z and lower is the pK\(_a\).
The Concept of Acidity and Basicity in Organic Chemistry

Effect of structure on acid and base strength of organic molecules:

C] Resonance Effect: The effect of different electron-withdrawing groups on the $pK_a$ value is demonstrated amply in the following table:

<table>
<thead>
<tr>
<th>Z</th>
<th>$pK_a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{CH}_3$</td>
<td>50</td>
</tr>
<tr>
<td>$\text{Me}$</td>
<td>20</td>
</tr>
<tr>
<td>$\text{C} \equiv \text{N}$</td>
<td>25</td>
</tr>
<tr>
<td>$\text{COEt}$</td>
<td>23</td>
</tr>
<tr>
<td>$\text{NMe}_2$</td>
<td>30</td>
</tr>
<tr>
<td>$\text{NO}_2$</td>
<td>10.2</td>
</tr>
</tbody>
</table>

Clearly, the greater the electron-withdrawing power of Z is, greater is the acidity of MeCH$_2$Z and lower is the $pK_a$.

A case in point is the relative acidity of ketone, ester and amide. As evident from $pK_a$ values, protons $\alpha$- to the ketones are generally more acidic than those $\alpha$- to an ester carbonyl, which are, in turn, more acidic than those $\alpha$- to amide carbonyls.

The resonance stabilization gained by ionization of the C($\alpha$)-H bond in increasingly lower as we move from ketone to amide via ester, because the ‘O’ and ‘N’ atoms in ester and amide molecules, respectively are involved in the resonance with the carbonyl in the non-dissociated acid prior to the ionization of the C-H bond. As N is less electronegative than O and more agreeable to release its electron pair, the resonance stabilisation in amide is greater than that in ester. Subsequently the gain in resonance stabilisation upon proton removal is less for the amide, resulting in its lower acidity than the ester.

Another point needs to be considered here that the conjugate bases from the ester and amide are cross-conjugated, thus offering little incentive for their formation from the resonance perspective, but the enolate from a ketone is not so and is formed to a greater extent at equilibrium.
The Concept of Acidity and Basicity in Organic Chemistry

Effect of structure on acid and base strength of organic molecules:

C] Resonance Effect: It stands to reason that if we introduce one more electron-withdrawing group to the same carbon, the acidity of the corresponding methylene group will increase farther, as the dispersion of negative charge of the conjugate base will be better through resonance.

This is indeed found to be the case. Consider the acidity of acetylacetone (2,4-hexanedione), where the methylene group is flanked by two keto groups, and consequently, has a pKa of 8.84, much lower than that of acetone.

It is obvious that acetylacetone has two different types of protons, one set on the methyl carbons while the other on the methylene carbon.

HW: Convince yourself that the latter is more acidic by drawing the respective conjugate bases and check for resonance stabilisation in them.

The same effect is observed with groups capable of exerting strong -R effect. Some of these carbon acids are so strong that they can actually act as acids in water. The following pKa values are instructive in this regard:

When we have a carbon is flanked by two strongly EW groups, such as carbonyl, nitro or cyano, the compound is known as an active methylene compound, reflecting its high acidity. The differential abilities of various electron-withdrawing groups are manifested in the wide range of the pKa values.
The Concept of Acidity and Basicity in Organic Chemistry

Effect of structure on acid and base strength of organic molecules:

C) Resonance Effect: From the above study we can say that the greater the dispersion of negative charge over the conjugate base of an acid is through resonance, higher is the acidity of the acid.

Thus we have the following observations:

\[
\begin{align*}
\text{H}_3\text{C} & \text{CH}_3 \\
pK_a & 21 \\
\text{MeO} & \text{O} \\
pK_a & 8.84 \\
\text{Me} & \text{O} \\
pK_a & 5.8 \\
\text{H}_2\text{C} & \text{C} \equiv \text{N} \\
pK_a & 25 \\
\text{H}_2\text{C} & \text{C} \equiv \text{N} \\
pK_a & 11 \\
\text{H}_2\text{C} & \text{C} \equiv \text{N} \\
pK_a & -5 \\
\end{align*}
\]

An interesting observation is the ever-decreasing influence of the EW groups when introduced one after the other in determining the acidity, i.e. the effect of the first group is much larger than the second which in turn is larger than the third.

In the series comprising toluene, diphenylmethane and triphenylmethane, this trend is most prominent. Methane has a \( pK_a \) value of about 52, while that of toluene is 41, so addition of the first phenyl ring increases the acidity by \( 10^{11} \) times, the second by \( 10^8 \) (\( pK_a \) of diphenylmethane is 33), and the third by only \( 10^2 \) (\( pK_a \) of triphenylmethane is 31).

The large shift of \( pK_a \) between toluene and diphenylmethane is obviously due to the additional resonance effect of the conjugate base by the introduction of the second phenyl ring. However, the third additional phenyl ring has a very small acid strength-enhancing effect. To explain the smallness of this change, several factors may be cited.

One is that the three phenyl rings cannot all be coplanar with the anionic carbon (because the \( \alpha \)-hydrogens of adjacent rings interfere sterically), which is required for the full resonance stabilization and instead a propeller-twist develops in the anion. This is an example of steric inhibition of resonance.

This loss of resonance implies that acid strength should not increase to the same extent as it does after the introduction of the first phenyl ring. The effect of this distortion can be seen by comparing the acidity of diphenylmethane (\( pK_a \) ca. 33), with fluorene (\( pK_a \) ca. 23), the latter has two rings tied together by removal of the offending ortho-hydrogens, an arrangement that ensures coplanarity and efficient conjugation.
The Concept of Acidity and Basicity in Organic Chemistry

Effect of structure on acid and base strength of organic molecules:

C) Resonance Effect: From the above study we can say that the greater the dispersion of negative charge over the conjugate base of an acid is through resonance, higher is the acidity of the acid.

Thus we have the following observations:

\[
\begin{align*}
\text{H}_3\text{C}=\text{C} & \quad \text{Me} & \quad \text{Me} & \quad \text{Me} \\
\text{O} & \quad \text{O} & \quad \text{O} & \quad \text{Me} \\
pK_a & \quad 21 & \quad 8.84 & \quad 5.8
\end{align*}
\]

Introduction of the second EW group generally does not affect the acidity of the carbon acid as much as the first one does. Again, the third substituent is found to affect acidity even less.

\[
\begin{align*}
\text{C} & \quad \text{C} & \quad \text{H}_2 \\
\text{Me} & \quad \text{C} & \quad \text{C} \\
pK_a & \quad 41.2 & \quad 33
\end{align*}
\]

The diminutive acid-strengthening effect of the second and third EW substituent is probably a result of the loss of conjugation in the successive conjugate bases due to steric inhibition of resonance.

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{N} & \quad \text{N} \\
\text{N} & \quad \text{C} & \quad \text{C} \\
pK_a & \quad 25 & \quad 11 & \quad -5
\end{align*}
\]

If the steric inhibition of resonance is absent in the conjugate bases, the successive EWGs may exert their full effect to enhance the acidity of the corresponding acids.

A case in point is acetonitrile, dicyanomethane and tricyanomethane. Note that the second and the third cyanide groups enhance the acidity to almost same extent. This indicates that conjugative electron withdrawal is not compromised in any of the conjugate bases.

As cyanide is linear in shape, one group does not interfere sterically with the other and they delocalise the charge harmoniously in all the conjugate bases, enhancing the acidity almost uniformly with each substitution.