Organic Chemistry-2

Semester-2, CBCS

Course: CEMA CC-2-3-TH

Course taught by: Kaushik Basu, Department of Chemistry, SPCMC, Kolkata
email: chiralkaushik@gmail.com

Recommended texts:

The Concept of Acidity and Basicity in Organic Chemistry

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

A] Periodic table correlations:

Acidity increases while basicity decreases on moving from left to right along the row (period) of the periodic table, for example,

<table>
<thead>
<tr>
<th>Acids</th>
<th>CH₄</th>
<th>NH₃</th>
<th>H₂O</th>
<th>HF</th>
</tr>
</thead>
<tbody>
<tr>
<td>(pK_a)</td>
<td>&gt;50</td>
<td>34</td>
<td>15.74</td>
<td>3.17</td>
</tr>
</tbody>
</table>

Acidity increases

Conjugate bases:

Conjugate bases: \(\text{CH}_3\), \(\text{NH}_2\), \(\text{OH}\), \(\text{F}\)

Basicity decreases

Electronegativity (Pauling scale): C (2.55) < N (3.04) < O (3.44) < F (3.98)

This trend can be explained by considering that on moving from left to right the electronegativity of the central atom increases, leading to a greater tendency to give up a proton.

For the conjugate bases, on moving from left to right the electronegativity of the central atom increases which results in a decreasing tendency for the conjugate base to regain the proton and thus the basicity decreases.

In the same vein, we have the following observation:

\[ \text{R}^+ - \text{C} = \text{O} - \text{H}_2 \]
\[ \text{R}^+ - \text{C} = \text{O} - \text{H} \]
\[ \text{R}^+ - \text{C} = \text{O} \]

\(pK_a\) 20-21 17 3.9

Acidity increases

Conjugate bases:

Electronegativity (Pauling scale): C (2.55) < N (3.04) < O (3.44)

However, in this case another important factor, namely the resonance stabilization of the corresponding conjugate bases must also be carefully considered.

But, that is a topic we will take up later.

Suffice to say here that along with other factors, the electronegativity of the atom bearing the negative charge plays its role in determining the relative acidity.
The Concept of Acidity and Basicity in Organic Chemistry

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

A) Periodic table correlations:

On moving down a column (group) of the periodic table, the acidity increases and basicity decreases despite the decrease in electronegativity of the central atom, for example,

\[
\begin{align*}
\text{HF} & : 3.17 \\
\text{HCl} & : 7 \\
\text{HBr} & : 9 \\
\text{HI} & : 10
\end{align*}
\]

The acidity increases as the conjugate base basicity decreases.

Conjugate bases:

\[\text{F}^- \quad \text{Cl}^- \quad \text{Br}^- \quad \text{I}^-\]

To explain this, we need to consider the basicity of the conjugate bases which are: \(\text{F}^-\), \(\text{Cl}^-\), \(\text{Br}^-\), and \(\text{I}^-\) respectively.

On moving from left to right in the series, the size of the anions increases, for which electron density decreases.

\[
\text{F}^- < \text{Cl}^- < \text{Br}^- < \text{I}^-
\]

Ionic radius increases: \(\text{F}^- > \text{Cl}^- > \text{Br}^- > \text{I}^-\)

Charge density increases.

As a result, the tendency of the conjugate base to regain the proton decreases. However, several other factors, such as solvation etc., are responsible for the above order of acidity, but we will come back to those later.

Let us consider the following order of basicity:

\[
\text{NH}_3 : \text{PH}_3 : \text{AsH}_3
\]

The basicity decreases as the size of the central atom increases, thus the electron density on the central atom decreases and the tendency to accept a proton gets lowered.

However, several other factors such as the % of s- and p-character of the lone pair, hardness-softness of the central atom etc. are also in operation here.
The Concept of Acidity and Basicity in Organic Chemistry

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

B. Effect of hybridization:

We have the following order of acidity:

\[
\begin{align*}
    & \text{H}_3\text{C}==\text{CH}_3 & \text{H}_2\text{C}==\text{CH}_2 & \text{HC}==\text{CH} \\
    \text{pK}_a & \text{ca. 50} & 44 & 25 \\
    \text{acidity increases}
\end{align*}
\]

To explain this we have to think about the basicity of the respective conjugate bases. Let us consider the different conjugate bases:

<table>
<thead>
<tr>
<th>The conjugate base (cB) from...</th>
<th>cBs are...</th>
<th>In cBs lone pair of electrons is in...</th>
</tr>
</thead>
<tbody>
<tr>
<td>ethane</td>
<td>(\text{H}_3\text{C}==\text{CH}_2)</td>
<td>sp(^3) hybrid orbital</td>
</tr>
<tr>
<td>ethylene</td>
<td>(\text{H}_2\text{C}==\text{C}==\text{H})</td>
<td>sp(^3) hybrid orbital</td>
</tr>
<tr>
<td>acetylene</td>
<td>(\text{H}==\text{C}==\text{C}==\text{H})</td>
<td>sp hybrid orbital</td>
</tr>
</tbody>
</table>

On moving downward the series of conjugate bases, the s-character of the hybrid orbitals, which contain the lone pair of electrons, increases, while \(p\)-character of the hybrid orbital decreases.

Recall that s-electrons are nearer to the positively-charged nucleus. As the relative s-character decreases, orbital size increases. So electrons in a sp-hybrid orbital will be held up more tightly than those in a sp\(^3\)-hybrid orbital.

Thus lower will be the tendency to regain a proton as we traverse down the above series, i.e., the basicity of the conjugate bases decreases. Thus we have the above order of acidity.
The Concept of Acidity and Basicity in Organic Chemistry

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

B] Effect of hybridization:

In the same line, any proton of cyclopropane is more acidic ($pK_a$ 46) than the methylene protons of propane ($pK_a$ 50).

The special case of cyclopropane:

- head-on overlap along the C-C internuclear axis means 60-degree angle - bad
- orbital with higher s-character

Consequence: bent bonds, electron density not between the C-C bonds, but outside the three-membered ring (see EPM), C-C bonds have more than usual p-character, and C-H bonds have more than normal s-character. C-C bond is unusually weak, C-H bond is unusually strong.

When we say more than normal, we compare the situation with a sp$^3$ hybridised carbon.

<table>
<thead>
<tr>
<th>Bond Character</th>
<th>Bond Strength</th>
<th>BDE (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-H bond has high s-character</td>
<td>stronger bond than normal</td>
<td>108</td>
</tr>
<tr>
<td>C-C bond has high p-character</td>
<td>weaker bond than normal</td>
<td>65</td>
</tr>
</tbody>
</table>

As the conjugate base from cyclopropane has the lone pair in an orbital that has higher s-character than the lone pair-carrying orbital in the conjugate base from propane, the acidity of cyclopropane is more.
The Concept of Acidity and Basicity in Organic Chemistry

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

B) Effect of hybridization:

\[
\begin{align*}
R_3\text{N} & \quad \text{basicity decreases} \\
pK_{aH} & \approx 10.5 \\
5.23 & \quad \text{means}
\end{align*}
\]

The hybridization of the N-atom must be considered here.

In \( R_3\text{N} \), the nitrogen lone pair is in an \( sp^3 \) hybrid orbital.

And in case of pyridine it is in an \( sp^2 \) hybrid orbital.

We know that electrons in \( sp^2 \) orbitals are more tightly held up than the electrons in \( sp^3 \) orbitals because of the greater s-character in the former.

Therefore, it is more difficult to donate the lone pair form an \( sp \) hybrid orbital compared to donating from an \( sp^3 \) hybrid orbital.

Thus moving from the aliphatic amine to pyridine, the tendency to accept a proton decreases. Thus we have the above order of basicity.
The Concept of Acidity and Basicity in Organic Chemistry

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

C] Inductive and field effect:

Let us consider the acidity of the following compounds:

\[
\begin{align*}
\text{H}_3\text{C}-\text{CO}_2\text{H} & \quad \text{pK}_a = 4.76 \\
\text{O}_2\text{N}-\text{C}-\text{CO}_2\text{H} & \quad \text{pK}_a = 1.68
\end{align*}
\]

acidity increases

cB: \[ \begin{align*}
\text{H}_3\text{C}-\text{CO}_2\text{O}^- & \\
\text{O}_2\text{N}-\text{C}-\text{CO}_2\text{O}^- &
\end{align*} \]

To explain this we have to consider the basicity of the conjugate bases.

For the conjugate base of nitroacetic acid \(\text{O}_2\text{NCH}_2\text{COO}^-\), the -I effect of electron-withdrawing nitro group assists in dispersion of negative charge over the carboxylate anion.

Thus this conjugate base has a lower tendency to regain the proton compared to \(\text{CH}_3\text{COO}^-\), the conjugate base of \(\text{CH}_3\text{COOH}\).

Thus nitroacetic acid is more acidic than acetic acid, as evident from the \(\text{pK}_a\) values.

Other electron-withdrawing groups such as \(\text{R}_3\text{N}^+\), CN, \(\text{SO}_2\text{R}\), CO, \(\text{CO}_2\text{R}\) increase the strength of simple aliphatic carboxylic acids as also do hydroxy and methoxy groups.

The unshared electrons on the oxygen atom of the last two groups are not capable to exert a +R effect, in opposite direction to their -I effect, owing to the intervening saturated carbon atom. Thus we have the following \(\text{pK}_a\) values:

<table>
<thead>
<tr>
<th>R</th>
<th>H⁻</th>
<th>Me₃N⁻</th>
<th>N≡C⁻</th>
<th>EtO⁻</th>
<th>Me⁻</th>
<th>H₂CO⁻</th>
<th>HO⁻</th>
</tr>
</thead>
<tbody>
<tr>
<td>pKₐ</td>
<td>4.76</td>
<td>1.83</td>
<td>2.47</td>
<td>3.35</td>
<td>3.58</td>
<td>3.53</td>
<td>3.83</td>
</tr>
</tbody>
</table>

cB: \[ \begin{align*}
\text{H}_2\text{C}-\text{CO}_2\text{O}^- & \\
\text{R}-\text{C}-\text{CO}_2\text{O}^- &
\end{align*} \]

if \(R\) is inductively EW in nature, \(\text{pK}_a\) of \(\text{RCH}_2\text{CO}_2\text{H}\) < \(\text{pK}_a\) of \(\text{CH}_3\text{CO}_2\text{H}\)

if \(R\) is inductively ER in nature, \(\text{pK}_a\) of \(\text{RCH}_2\text{CO}_2\text{H}\) > \(\text{pK}_a\) of \(\text{CH}_3\text{CO}_2\text{H}\)

\[\text{shows -I effect...}\]

\[\ldots\text{helps in delocalizing the negative charge, increases the acidity of R-CH}_2\text{COOH compared to H-CH}_2\text{COOH}\]
The Concept of Acidity and Basicity in Organic Chemistry

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

C) Inductive and field effect:

- Shows -I effect...
  \[ R\text{-CH}_2\text{COOH} \]
  ...helps in delocalizing the negative charge, increases the acidity of \( R\text{-CH}_2\text{COOH} \) compared to \( \text{H-CH}_2\text{COOH} \)
  \[ \text{cB: } R\text{-CH}_2\text{COO}^{-} \]

- Shows +I effect...
  \[ R\text{-COOH} \]
  ...helps in intensifying the negative charge, decreases the acidity of \( R\text{-CH}_2\text{COOH} \) compared to \( \text{H-CH}_2\text{COOH} \)
  \[ \text{cB: } R\text{-C}^{-} \]

If \( R \) is inductively EW in nature, \( pK_a \) of \( \text{RCH}_2\text{CO}_2\text{H} \) < \( pK_a \) of \( \text{CH}_2\text{CO}_2\text{H} \)
If \( R \) is inductively ER in nature, \( pK_a \) of \( \text{RCH}_2\text{CO}_2\text{H} \) > \( pK_a \) of \( \text{CH}_2\text{CO}_2\text{H} \)

Let us consider the acidity of the following compounds:

\[
\begin{align*}
\text{H}_3\text{C-}-\text{CO}_2\text{H} & \quad pK_a = 4.76 \\
\text{H}_3\text{C-}'-\text{CO}_2\text{H} & \quad pK_a = 4.86
\end{align*}
\]

Acidity decreases

Me is an ERG, shows +I effect

Let us consider the acidity of the following compounds:

\[
\begin{align*}
\text{H}_3\text{C-}-\text{CO}_2\text{H} & \quad pK_a = 4.76 \\
\text{H}_3\text{C'-}-\text{CO}_2\text{H} & \quad pK_a = 3.77
\end{align*}
\]

Acidity increases

But the acidity difference is not a result of only the electronic effect, there is solvation effect operating as well.

Me is an ERG, shows +I effect

How to understand the solvation effect on acidity?

The acidity of an acid improves as its cb gets more solvated, as the negative charge is more and more dispersed by the solvent. This should be an intuitive result (do you agree?).

The methyl group is hydrophobic (water-hating) in nature so the acetate ion is less solvated in aqueous medium in which the acid strength is being measured. This means that while the acetate ion suffers from lack of solvation in aqueous medium, the formate ion is much more solvated.

Thus the acetate ion will have a greater tendency to regain a proton than the formate ion, implying that the former's basicity is higher. This in another way of saying that acetic acid is a weaker acid than formic acid, as suggested by the \( pK_a \) data.

Study Guide to Organic Chemistry
- Saha et al. Volume 2 (ISBN 9788192669588)
The Concept of Acidity and Basicity in Organic Chemistry

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

C) Inductive and field effect:

We can also infer from the above study that with an increase in the inductive electron withdrawing effect, the acidity is expected to increase. Thus we have the following observation:

\[
\begin{align*}
\text{Cl} & \text{COOH} & \text{Cl} & \text{COOH} & \text{Cl} & \text{Cl} & \text{COOH} & \text{F} & \text{F} & \text{COOH} \\
pK_a & 2.85 & 1.25 & 0.66 & 0.23 \\
\end{align*}
\]

acidity increases as the number of EW chlorine atoms increase and it is highest in the series when more electronegative fluorine is present instead of chlorine.

F is more electronegative than Cl, CF\textsubscript{3} has a greater -I effect than CCl\textsubscript{3}

Molecular electrostatic potential (MEP) maps of a) acetate and b) trichloroacetate - you can clearly see that the negative charge is more delocalized (less dense red colour) in the latter, due to the inductive EW effect of the CCl\textsubscript{3} group.

As inductive effect is known to decrease with increasing distance between the group that exerts the effect and the position where the effect is experienced, it is expected that the acidity of the halogen-substituted carboxylic acids will decrease as the distance between the halogen atom and the carboxylic acid group increases.

\[
\begin{align*}
\text{Me} & \text{C} & \text{H} & \text{O} & \text{H} & \text{Me} & \text{C} & \text{H} & \text{Cl} & \beta & \text{O} & \text{H} & \text{Cl} & \gamma & \text{O} & \text{H} \\
pK_a & 4.85 & 2.85 & 4.05 & 4.50 \\
\end{align*}
\]

The EW effect is most pronounced when the electron-withdrawing group is located at the \(\alpha\)-position (C-2). As the distance between the chlorine atom and the carboxylic acid group increases, the EW effect of the chlorine atom is diminished, acidity decreases.
The Concept of Acidity and Basicity in Organic Chemistry

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

C) Inductive and field effect:

Field effect: While inductive effect involves polarisation through a network of sigma bonds, field effect is said to involve polarisation through space or through solvent molecules that occupy the space between the group that is showing the effect and the part of the molecule that is experiencing that effect.

It is rather difficult to separate the field effect from the inductive effect, but one important point of difference between the two is that the field effect depends upon the geometry of the molecule, while inductive effect’s effectiveness depends on the number of sigma bonds that separate the group exerting the inductive effect and the site that is experiencing the effect. This allows us to sometimes separate field effect from inductive effect. Consider the following example:

In isomers 1 and 2, the inductive effect of the chlorine atoms on the position of the electrons in the COOH group (and hence on the acidity) should be the same since in both cases, the number of intervening bonds is the same.

The number of intervening bonds between the carboxylate and two chlorine atoms in both conjugate bases are highlighted in blue. So inductive effect should be same. Any stabilization by the cBs by inductive effect should be same for two isomers.

But the field effect of the Cl atoms should be different in the two isomers because the chlorines are closer in space to the COOH in 1 than they are in 2. Thus a comparison of the acidity of 1 and 2 should reveal whether a field effect is truly operating.

We can see that isomer-1 is less acidic than isomer-2. This difference of acidity between isomers-1 and 2 can be explained by considering the respective conjugate base’s stability by different field effects.

From the data given that isomer-1 is less acidic than isomer-2, the cB of isomer-1 should be less stable than the cB of isomer-2.
This relative destabilisation is explained by the field effect of the Cl atoms in the following way:

The dipole associated with the polar C-Cl bond