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

Preliminary concepts: What is an acid and what is a base? And how do we compare the relative strengths of series of acids and series of bases?

To understand what is meant by the questions posed immediately above, we need to consider the definitions of acids and bases provided independently by Johannes Nicolaus Brønsted and Thomas Martin Lowry way back in 1923.

The Brønsted-Lowry theory says that an acid is a substance which can give up a proton and a base is a substance which can accept a proton.

In simple terms, an acid is thus defined as a proton donor and a base as a proton acceptor and an acid-base reaction is simply the transfer of a proton from an acid to a base.

Let us consider the following simple reaction:

\[ \text{HCl} + \text{NH}_3 \rightarrow \text{NH}_4^+ + \text{Cl}^- \]

Here hydrogen chloride gives up a proton to ammonia to form ammonium chloride.

Thus hydrogen chloride is an acid and ammonia is a base.

Under suitable condition, however, the ammonium ion can act as a proton donor i.e. it can act as an acid.

A case in point is the laboratory preparation of ammonia.

\[ 2 \text{NH}_3\text{Cl} + \text{Ca(OH)}_2 \xrightarrow{\text{heat}} \text{CaCl}_2 + 2 \text{NH}_3 + 2 \text{H}_2\text{O} \]

Similarly, under proper condition the chloride ion can accept a proton i.e. it can act as a base, e.g. the laboratory preparation of hydrogen chloride.

\[ 2 \text{NaCl} + \text{H}_2\text{SO}_4 \xrightarrow{\text{heat}} 2 \text{HCl} + \text{Na}_2\text{SO}_4 \]

Thus ammonium ion is called a conjugate acid of the base ammonia and chloride ion is referred to as the conjugate base of the acid hydrogen chloride.

\[ \text{Cl}^- + \text{H}^+ + \text{NH}_3 \rightarrow \text{NH}_4^+ + \text{Cl}^- \]

(acid) (acid) (conjugate acid) (conjugate base, of NH\textsubscript{3}) (conjugate base, of HCl)

Therefore, all acids have a conjugate base, and all bases have a conjugate acid. All acid-base reaction thus corresponds to the following equation:

\[ \text{An acid} + \text{A base} \rightarrow \text{A conjugate base of the acid} + \text{A conjugate acid of the base} \]
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The Brønsted-Lowry theory of acids and bases:

\[
\text{Cl}^-\text{H}^+ + \text{NH}_3 \rightarrow \text{NH}_4^+ + \text{Cl}^- \\
\text{(acid)} \quad \text{(base)} \quad \text{(conjugate acid, } cA, \text{ of NH}_3) \quad \text{(conjugate base, } cB, \text{ of HCl)}
\]

Therefore, all acids have a conjugate base, and all bases have a conjugate acid. All acid-base reaction thus corresponds to the following equation:

An acid + A base \rightarrow A conjugate base of the acid + A conjugate acid of the base

The Brønsted-Lowry theory can be logically extended by saying that:

higher the tendency to give up a proton, higher is the acidity of the concerned acid
and
higher the tendency to accept a proton, higher is the basicity of the corresponding base.

Thus, for the given reaction where hydrogen chloride protonates ammonia to afford ammonium ion and chloride ion, we must say:

\[
\text{Cl}^-\text{H}^+ + \text{NH}_3 \rightarrow \text{NH}_4^+ + \text{Cl}^- \\
\text{(acid)} \quad \text{(base)} \quad \text{(conjugate acid, } cA, \text{ of NH}_3) \quad \text{(conjugate base, } cB, \text{ of HCl)}
\]

\[\text{If the ammonium ion had a greater tendency than hydrogen chloride to give up proton, and chloride had a greater tendency than ammonia to accept a proton, then we would have seen the ammonium protonating the chloride to afford ammonia and hydrogen chloride. But that is not the case.}\]

Therefore, we must say that:

HCl is a stronger acid than NH\(_4^+\) and NH\(_3\) is a stronger base than Cl\(^-\)

Thus according to the Brønsted-Lowry theory:

A strong acid + A strong base \rightarrow A weak conjugate base of the acid + A weak conjugate acid of the base

As a result, we can say that acid-base reactions will only proceed in the forward direction if the acid (e.g. hydrogen chloride) and the conjugate acid of the base (ammonium) have different strength and the former is more acidic than the latter.
The Concept of Acidity and Basicity in Organic Chemistry

Effect of Solvents on Acids and Bases:

A compound can act as either an acid or as a base in different solvents. Let us consider the following equilibrium:

\[
\text{Ph-NH}_2 + \text{Me-C} = \text{O} \text{OH} \rightleftharpoons \text{Ph-N}^+ + \text{Me-C} = \text{O}^{-} \]

\[
\text{Ph-NH}_2 + \text{NH}_3 \text{ (liq)} \rightleftharpoons \text{Ph-N}^- + \text{NH}_4^+ \]

Thus aniline acts as a base in acetic acid whereas it acts as an acid in liquid ammonia.

\[
\text{Me-C} = \text{O} \text{OH} + \text{H}_2\text{O} \rightleftharpoons \text{Me-C} = \text{O}^{-} + \text{H}_3\text{O}^+ \]

\[
\text{Me-C} = \text{O} \text{OH} \text{H}_2\text{SO}_4 \rightleftharpoons \text{Me-C} \text{OH} + \text{HSO}_4^- \]

Acetic acid acts as an acid in water while in sulphuric acid it acts as a base.

Thus the acid-base property of a compound can be related on the relative proton affinity of the substance and the solvent in which it is taken. Higher the proton affinity, higher is the basicity.

Let us turn to another aspect of solvent effect towards acidity and basicity.

In aqueous medium carboxylic acids usually do not transfer proton completely to water - which is the solvent:

\[
\text{R-C} = \text{O} \text{OH} + \text{H}_2\text{O} \rightleftharpoons \text{R-C} = \text{O}^{-} + \text{H}_3\text{O}^+ \]

But in liquid \text{NH}_3 carboxylic acids transfer proton completely to the ammonia molecule:

\[
\text{R-C} = \text{O} \text{OH} + \text{NH}_3 \rightleftharpoons \text{R-C} = \text{O}^{-} + \text{NH}_4^+ \]

This can only mean that ammonia is more basic than water.

Evidently, the effective acidic species in liquid ammonia is the ammonium ion, \text{NH}_4^+.

Thus all carboxylic acids that transfer their protons completely to ammonia molecule have similar acid strength in the liquid ammonia solvent. This is called the "Levelling Effect" of ammonia on carboxylic acids.

Similarly, \text{Hl}, \text{HBr} and \text{HCl} are equally strong acids in water - as all of these acids completely transfer their protons to water.

Undoubtedly, in this case the effective acid is \text{H}_3\text{O}^+. Here the halogen acids experience the Levelling Effect of water.

In the same token, \text{KNH}_2 and \text{KOCMe}_3 have equal base strength in water - as these deprotonate water completely to yield hydroxide ion which is the effective base. Thus here we can say that there is operating a Levelling Effect of water on \text{KNH}_2 and \text{KOCMe}_3.
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Effect of Solvents on Acids and Bases:

The above study indicates that to distinguish between the strengths of different acids we have to use a solvent whose basicity will be such that there will be an incomplete transfer of proton from the acid to the solvent.

Similarly, to differentiate the strengths of bases we have to use a solvent such that there will be only partial transfer of proton from the base to the solvent.

Only if this condition is met, the extents of proton transfer will be different for two acids, or two bases, as the case may be, and we will have an estimate of the relative strengths of the different acids and different bases.

Thus, if we use water as the solvent where mineral acids transfer their proton completely while carboxylic acid does so only partly, we will find that mineral acids are stronger than carboxylic acids.

We can use water also to differentiate the strengths of different carboxylic acids which protonate water to different extents. But we cannot use water to compare the strengths of different mineral acids as all of them will protonate water completely.

In contrast, in methyl alcohol HCl transfers proton completely but HNO₂ does not. So HCl is a stronger acid than HNO₂ in methanol.

Acidity or basicity of a solvent, however, is not the only aspect that controls the acidic or basic strength of the acid or base under consideration.

Solvation effect is significant as well.

For example, when KOH is dissolved in methanol, a polar and protic solvent, both K⁺ and OH⁻ are solvated by methanol molecules - but when KOH is dissolved in dimethyl sulfoxide (DMSO, Me₂SO, a polar aprotic solvent) only K⁺ is solvated by DMSO but not OH⁻. So, due to this lack of solvation, OH⁻ is much stronger base in DMSO than that in water. Thus we have the following observations when sodium methoxide in taken in two different solvents:

\[
\text{Me, } \text{HCl-Br} \quad \xrightarrow{\text{NaOMe, MeOH}} \quad \text{MeC=CH}_2 \quad \text{relative rate} = 1.0
\]

\[
\text{Me, } \text{HCl-Br} \quad \xrightarrow{\text{NaOMe, DMSO}} \quad \text{MeC=CH}_2 \quad \text{relative rate} > 10^3
\]

The methoxide ion functions as a much stronger base in DMSO medium than it does in methanol. It is pertinent to mention here that protic solvents are those that can act as H-bond donors to anions, subsequently solvating them while aprotic solvents are those than cannot act as H-bond donors.
The Concept of Acidity and Basicity in Organic Chemistry

A Method of Quantifying Acid-Base Strength: The concept of $pK_a$ and $pK_{ah}$

To measure the strength of acid and base, the extents of proton transfer of the same in water are used.

Acids: Let us consider the following equilibrium where an acid H-A is dissociated in water. Here water acts as the base. $A^-$ is the conjugate base of acid HA, and $H_3O^+$ (hydronium ion) is the conjugate acid of water. Evidently, the more the equilibrium lies towards the right hand side, i.e. more the hydronium ion in water, higher is the acidity of H-A.

$$H^-A \text{(aq.)} + H_2O \text{(l)} \rightleftharpoons H_3O^+ \text{(aq.)} + A^- \text{(aq.)}$$

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

The concentration of water, $[H_2O]$, remains essentially constant at 55.56 mol dm$^{-3}$ with dilute solutions of acid irrespective of the position of equilibrium, because it is present in a large excess; therefore, we can introduce a new equilibrium constant $K_a$ in which $[H_2O]$ has been incorporated. $K_a$ is called the acidity constant (or acid dissociation constant or acid ionization constant) and is defined as:

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

Now, higher the $K_a$, higher is the acidity of HA. But these data are impracticable to handle as they spread over many orders of magnitude. For example, acetic acid has an acidity constant $1.75 \times 10^{-5}$. To avoid dealing with such cumbersome data, $K_a$ is conveniently expressed in logarithmic form $pK_a$, where $pK_a = -\log K_a$ (recall pH in this regard!).

Thus the $pK_a$ of acetic acid is $-\log (1.75\times10^{-5}) = 4.76$. Because of the presence of minus sign in its definition, lower $pK_a$ implies larger $K_a$, and thus higher acidity. Therefore, when comparing the acid strength of two acids, the one which has a lower $pK_a$ is the stronger acid than the other.
The Concept of Acidity and Basicity in Organic Chemistry

A Method of Quantifying Acid-Base Strength: The concept of $pK_a$ and $pK_{aH}$

To measure the strength of acid and base, the extents of proton transfer of the same in water are used.

Bases: Let us consider the following equilibrium where a base $B$ is deprotonating water. Here water acts as the acid, $BH^+$ is the conjugate acid of a base $B$, and $\cdot\cdot\cdot OH$ is the conjugate base of water. The more the equilibrium lies to the right, i.e. the more hydroxide ion is in water, greater is the basicity of $B$.

\[
\text{B(aq.) + H}_2\text{O(l)} \rightleftharpoons \text{BH}^{+}\text{ (aq.) + OH}^{-}\text{ (aq.)}
\]

Following the same principles as with acidity constant, we can now define the basicity constant $K_b$ as follows:

\[
K_b = K_{eq}\frac{[BH^+]}{[H_2O]} = \frac{[\cdot\cdot\cdot OH]}{[\cdot\cdot\cdot B]}
\]

Therefore, higher the $K_b$ value, higher is the basicity. But again due to the inconvenience in handling small values, we express $K_b$ in logarithmic scale, $pK_b = -\log K_b$. It implies therefore, that, the lower the $pK_b$ value, the higher is the basicity.

Since Brønsted-Lowry concept of acids and bases is associated with proton transfer, it is convenient to replace $pK_b$ of $B$ with the $pK_a$ of the conjugate acid $BH^+$ (better known as $pK_{aH}$, to avoid possible ambiguity in case of amphoteric compounds like ammonia). Thus,

\[
\text{BH}^{+}\text{ (aq.) + H}_2\text{O(l)} \rightleftharpoons \text{B(aq.) + H}_3\text{O}^{+}\text{ (aq.)}
\]

\[
K_{aH} = \frac{[\cdot\cdot\cdot B]}{[\cdot\cdot\cdot H_3O^{+}]} = \frac{[\cdot\cdot\cdot B][H_2O]}{[BH^+]} \quad \text{and} \quad pK_{aH} = -\log K_{aH}
\]

Now,

\[
K_b \times K_{aH} = \frac{[BH^+][OH^-]}{[B]} \times \frac{[B][H_3O^+]}{[BH^+]} = [H_3O^+][OH^-] = K_w \quad \text{(ionic product of water) = 10^{-14} (at 25 °C)}
\]

Thus,

\[
-\log K_{aH} \quad \text{of BH}^+ - \log K_b \quad \text{of B} = -\log K_w
\]

\[
\therefore pK_{aH} \quad \text{of BH}^+ + pK_b \quad \text{of B} = pK_w = 14
\]

\[
\therefore pK_{aH} \quad \text{of BH}^+ = pK_w - pK_b \quad \text{of B}
\]

So lower the value of $pK_b$ of B is, higher the value is of $pK_{aH}$ of BH+, higher is the basicity of B.

The $pK_a$ of water is 15.74 while that for the conjugate acid $H_3O^+$ is -1.54. You might want to work out how these values are derived.
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Let us now revisit the effect of solvents on the pKₐ values of acids. It is important to note that the pKₐ values of acids are often higher in mediums such as DMSO than those in water. A case in point is benzoic acid:

\[ \text{pKₐ in water} = 4.2 \]
\[ \text{pKₐ in DMSO} = 11.1 \]

The conjugate base of this acid is the benzoate ion:

Because acid-base reactions are equilibriums, the greater the percentage population of the conjugate base present in the equilibrium, higher is the acidity, lower is the pKₐ.

If the solvents can effectively stabilize the anionic conjugate base, its percentage population in equilibrium will increase, leading to a higher acidity.

DMSO is a polar, aprotic solvent while water is a polar, protic one. The acid HA always has a lower propensity of ionizing in DMSO because the solvent offers little solvation to the conjugate base A⁻ (a hydrogen bond acceptor species) due to the solvent’s lack of H-bond donation capacity.

Water, on the other hand, stabilizes the anionic conjugate base more effectively than DMSO by forming hydrogen bonds with A⁻. Thus acid ionization equilibrium for acids such as HA is always less favoured in DMSO than in water, leading to the higher acidity and lower pKₐ in the latter solvent.

![Diagram showing solvation of A⁻ by water molecules through H-bonding](image-url)
The Concept of Acidity and Basicity in Organic Chemistry

The problem of predicting the relative acidity/basicity of different organic molecules: How to approach the problem:

Acidity and basicity are thermodynamic aspects of the position of equilibrium with respect to the transfer of proton.

Therefore, in order to explain the acidity and basicity order of a series of compounds, we basically need to consider the relative stabilities of acids and their conjugate bases and the relative stabilities of bases and their conjugate acids. From this, we have to make a qualitative prediction regarding the position of that acid-base equilibrium.

If the equilibrium is more favourable towards the right hand side of the equilibrium, for an acid that is on the left hand side, the acidity will be higher.

*Compared to what?*

Compared to another acid, for which the equilibrium is comparatively less favourable.

You have to be cautious in this analysis. This is only valid if both acids are compared w.r.t. the same base.

Let us consider an example:

\[
\begin{align*}
\text{phenol} + \text{H}_2\text{O} & \rightleftharpoons \text{phenoxide} + \text{H}_3\text{O}^+ \\
pK_a\ of\ phenol\ 9.98 & \quad \Rightarrow \quad K_a = 10^{-9.98} \\
\text{benzoic acid} + \text{H}_2\text{O} & \rightleftharpoons \text{benzoate} + \text{H}_3\text{O}^+ \\
pK_a\ of\ benzoic\ acid\ 4.2 & \quad \Rightarrow \quad K_a = 10^{-4.2}
\end{align*}
\]

It is understood that for both phenol and for benzoic acid, the respective equilibriums favour the LHS.

Yet, for benzoic acid, the equilibrium favours the RHS to a greater extent than the corresponding equilibrium for phenol does.

Hence, the pK_a of benzoic acid is lower than that of phenol and the former is the stronger acid of the two.

The take-home lesson from this is that the *equilibrium itself need not necessarily favour the RHS*, but *to what extent it lies towards the RHS compared to the other equilibrium* involving another acid settles the issue.

In the same token, a comparatively more favourable equilibrium towards the RHS for a base that is on the LHS implies higher basicity for that base. In this way we can discuss relative acidity and basicity orders of several series.
The Concept of Acidity and Basicity in Organic Chemistry

The problem of predicting the relative acidity/basicity of different organic molecules: How to approach the problem (contd.):

Acidity and basicity are thermodynamic aspects of the position of equilibrium with respect to the transfer of proton.

So, the question is, how can we form in our minds a qualitative idea about different acid-base equilibria?

Let us think about this carefully for a moment.

If the conjugate acid $X^-$ of any acid $HX$ has a lower tendency to regain a proton compared to another conjugate base $Y^-$ of another acid $HY$, then we can say that between $X^-$ and $Y^-$, the former is a weaker base.

Consequently, from Brønsted-Lowry theory, we can also safely say that $HX$ then should 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 -

The higher the dispersion of the negative charge density in the conjugate base, the lower is its tendency to regain the proton. The lower the tendency to regain a proton, the weaker is that conjugate base, and thus, higher is the acidity of the corresponding acid.

Similarly, basicity order is explained by considering the availability of the lone pair of electrons of the base in question - if it is more available, the basicity of the base is higher than any other base which is relatively reluctant to give away its electron pair.

Thus, for a comparison of acidity between phenol and benzoic acid,

\[
\text{\begin{align*}
\text{phenol} & \quad + \quad \text{H}_2\text{O} \\
pK_a \text{ of phenol} & \quad 9.98
\end{align*}}
\]

\[
\text{\begin{align*}
\text{benzoic acid} & \quad + \quad \text{H}_2\text{O} \\
pK_a \text{ of benzoic acid} & \quad 4.2
\end{align*}}
\]

Given the $pK_a$ values we must say that the benzoate is the weaker base than the phenoxide. This means that that benzoate has a lower tendency than phenoxide to abstract a proton. This means that the negative charge is more dispersed in the benzoate ion than it is in the phenoxide. Notice CAREFULLY that we have started from the $pK_a$ and worked our way backwards, i.e. we knew which one is the more acidic of the two. Now we have to correlate WHY benzoate is a weaker base than phenoxoide - i.e. why is the negative charge more dispersed in the former anion? That answer can only be found inspecting the structures of both the anions.

What if they do not give you the $pK_a$? You have to train yourself to guesstimate the various factors that control the acidity and basicity of organic compounds to make any reasonable prediction. We will discuss these factors now, one by one.

Let us now consider the different trends of acidity. But before we proceed, a note of caution. Acidity trends are hardly ever dependent on a single factor. Dispersal of negative charge may be a guiding principle but that too has a varying dependence on more than one factor in general. In the following sections we discuss these different factors one by one, so emphasis will be on that particular factor, but we have to remember that along with that, other factors are also in operation.