Consider Acidity and Basicity  Recall carboxylic acids and amines (base).

Jones: p 237-8; 149, 291, 822-826, 1086-1090, 958-963, 878-882

General terms:

Lewis acid: capable of accepting an electron pair to form a covalent bond.
prototype example: $\text{BF}_3$ empty orbital in valence shell

Lewis base: capable of donating an electron pair to form a covalent bond.
prototype example: $:\text{NH}_3$ low energy non-bonding electrons

In simplest case, non-bonding electron pair on Lewis base engages in overlap with empty atomic orbital on Lewis acid to form a "coordinate covalent bond".

Bronsted acid: capable of delivering a proton (special acid)
e.g., $\text{HCl}$

Bronsted base: capable of accepting a proton
e.g., $\text{NaOH}$ and $\text{NH}_3$

In general:  How does the structure of a molecule affect its acidity/basicity?

Define: equilibrium acidity:

$$
\text{H-A} \rightleftharpoons \text{H}^+ + \text{A}^- \\
K_{eq} = K_a = \frac{[\text{H}^+][\text{A}^-]}{[\text{HA}]}
$$

If the free energy ($\Delta G$) of the products is equal to the free energy of the reactants, $K_{eq} = 1$

If the products have a larger $-\Delta G$, more stable, and $K_{eq} > 1$

If the reactants have a larger $-\Delta G$, reactants are more stable and $K_{eq} < 1$

Usually express acidity in terms of $pK_a$, negative log of $K_a$.

What are the factors which influence the $pK_a$?

Remember Hess's law?

$$
\text{H-A} \rightarrow \text{H}^+ + \text{A}^- \quad \text{(bond dissociation energy)}
$$

$$
\text{A}^- + e^- \rightarrow \text{A}^{2-} \quad \text{electron affinity}
$$

$$
\text{H}^+ \rightarrow \text{H}^+ + e^- \quad \text{ionization potential}
$$

add up:

$$
\text{H-A} \rightarrow \text{H}^+ + \text{A}^-
$$

more electronegative: higher electron affinity (more easily form $\text{A}^-$; less easily add $\text{H}^+$ to $\text{A}^-$)

stronger H-A bond: higher BDE and less easy to ionize
Compare acidity (ease of ionization):

<table>
<thead>
<tr>
<th></th>
<th>H-F</th>
<th>H-OH</th>
<th>H-NH₂</th>
<th>H-CH₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>pKa</td>
<td>3.2</td>
<td>15.7</td>
<td>ca 35</td>
<td>&gt;55</td>
</tr>
<tr>
<td>EN</td>
<td>4.0</td>
<td>3.4</td>
<td>3.0</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Electronegativity has a big effect
(bond energies are similar, except the H-F bond is unusually strong)

Bond dissociation energies can dominate:

<table>
<thead>
<tr>
<th></th>
<th>H-F</th>
<th>H-Cl</th>
<th>H-Br</th>
<th>H-I</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDE</td>
<td>135</td>
<td>103</td>
<td>88</td>
<td>71</td>
</tr>
<tr>
<td>EN</td>
<td>4.0</td>
<td>3.2</td>
<td>3.0</td>
<td>2.7</td>
</tr>
<tr>
<td>pKa</td>
<td>3.2</td>
<td>-7</td>
<td>-9</td>
<td>-9.5</td>
</tr>
</tbody>
</table>

H-OH  \( \rightarrow \)  \( \text{H}^+ \) + \( \text{HO}^- \)  pKa 15.7

CH₃CH₂O-H  \( \rightarrow \)  CH₃CH₂O⁻ + \( \text{H}^+ \)  pKa 15.9 (a little less acidic)
ethoxide anion, the conjugate base of ethyl alcohol

Therefore: If mix NaOH with CH₃CH₂OH,
get approx. equal amounts of NaOH, NaOCH₂CH₃, H₂O, CH₃CH₂OH

Consider:

acidity:  \( \text{CF₃CH₂OH} > \text{CF₃CH₂CH₂OH} > \text{CF₃CH₂CH₂CH₂OH} > \text{CH₃CH₂OH} \)
pKa 12.4 14.6 15.4 15.9

CH₃CH₂OH  \( \rightarrow \)  CH₃CH₂O⁻ + \( \text{H}^+ \)  pKa 15.9
CF₃CH₂OH  \( \rightarrow \)  CF₃CH₂O⁻ + \( \text{H}^+ \)  pKa 12.4
\[ \Delta G_1 > \Delta G_2 \] Therefore, \( pK_a(1) \) is > \( pK_a(2) \)

ethyl alcohol is a weaker acid compared to 2,2,2-trifluoroethyl alcohol

\[ \Delta \Delta G = 2.3RT \left[ pK_a(1) - pK_a(2) \right] = (2.3) (2.0 \text{ cal mol}^{-1} \text{ K}^{-1}) (300^0 \text{K}) (15.9-12.4) = \]

ca 5000 cal/mol or 5 kcal/mol

Assume room temperature, 300\(^0\)K

Now: Why? What is responsible for the 5 kcal/mol lower energy difference?

Approximation: the concentration of charge in the anion is a dominant factor in determining whether proton loss is more-or-less favorable.

Analyze factors which influence the product after de-protonation: inductive effects, electronegativity

Focus on the ALKOXIDE ANION. (other differences are parallel--breaking O-H bond in both cases, no serious structural change, etc)

CF\(_3\)CH\(_2\)OH is more acidic than CH\(_3\)CH\(_2\)OH due to the inductive effect of the F substituent:

Very electronegative F draws electrons from adjacent carbon, transmitted to second carbon, and then to O\(^-\).
New observation: effects of branching on alcohol acidity

More methyl groups around carbon bearing the alkoxide anion,
less stable product,
less favorable ionization,
less acidic,
higher $pK_a$

Consider the extremes:
methyl alcohol

tertiary butanol, tert-butanol, t-butyl alcohol, 2-hydroxy-2-methylpropane, 2-methyl-2-propanol

Solvent is critical factor. Remove solvent? Gas phase acidities: Order is exactly reversed:

Stabilizing factors in the gas phase: polarizibility

larger atoms are more polarizable (carbon vs hydrogen)

NOTE: Assume reactions are generally taking place in a solvent, not gas phase.

Water is a "polar, protic" solvent High dielectric constant (78), Strong H-bonding
Dimethyl sulfoxide is a "polar, aprotic" solvent. High dielectric constant (47) NO H-bond donation HO\(^{-}\) not as well solvated

NaOH is a much stronger base in DMSO compared to water

Diethyl ether is a relatively non-polar (dielectric constant = 4.3), aprotic solvent. But it has non-bonding electrons available, it can be an electron donor:

Lewis acid/Lewis base opportunity with **cations:**

CROWN ETHERS  (Nobel prize 1992)

\[
\begin{align*}
\text{[18]-crown-6} & \quad \text{ethylene glycol} & \quad \text{octahedral geometry}
\end{align*}
\]

\[
\begin{align*}
\text{+ NaCl} & \quad \rightarrow \\
\end{align*}
\]

**NEW PARAMETER: DELOCALIZATION**

Compare:

\[
\begin{align*}
\text{H} & \quad \text{C} & \quad \text{O} & \quad \text{H} & \quad \leftrightarrow & \quad \text{H} & \quad \text{C} & \quad \text{O} & \quad \text{H} & \quad + & \quad \text{H}^{+} & \quad \text{pK}_{a} \quad 5
\end{align*}
\]

10 orders of magnitude difference in acidity

\[
\begin{align*}
\text{H} & \quad \text{H} & \quad \text{C} & \quad \text{O} & \quad \text{H} & \quad \leftrightarrow & \quad \text{H} & \quad \text{H} & \quad \text{C} & \quad \text{O} & \quad \text{H} & \quad + & \quad \text{H}^{+} & \quad \text{pK}_{a} \quad 15
\end{align*}
\]

The electron on the oxygen anion can be delocalized onto the other oxygen:
Good question: where are the electrons? Answer: spread over both oxygens equally, not at the C. Difficult to write conventional bonds to express this feature. The actual molecule is neither of the two "localized" structures, but the "average" of the two.

Note the arrangement of p orbitals available to the carboxylate anion:

**Acidity of Carboxylic Acids; Delocalization in the Anion:**

Two equivalent (in energy) resonance structures, both with all bonding possibilities filled. The extra electron pair is distributed over two O atoms, much better than when localized on one O. Strong resonance stabilization, strong delocalization. Therefore a carboxylic acid is $10^{10}$ more acidic than a simple alcohol; the product oxygen anion is much more stabilized and therefore forms much more easily.

**Acidity of Propene, Delocalization in the Anion:**

The dominant effect is the delocalization of charge.

Steric, Inductive, Resonance effects help to rationalize structure/acidity

Resonance picture:

Molecular Orbital analysis for allyl systems:

Consider the anion from propene:

MO picture: mix three p type atomic orbitals by linear combination $\Rightarrow$ three MOs

Jones, p 531.