Acids, Bases, Reactive Intermediates and Mechanisms
Ahrrenius Acid-Base Theory

– Acid
  • Source of H⁺ (H₃O⁺)
  • HCl + H₂O → H₃O⁺ + Cl⁻
  • HCl produces H₃O⁺

– Base
  • Source of HO⁻
  • NH₃ + H₂O → NH₄⁺ + HO⁻
  • NH₃ produces HO⁻

– OK for most acids in aqueous medium
– Does not describe carbon acids
– Does not apply in nonaqueous solvents
Brønsted Acid-Base Theory

- Focused on protons (H+)
  - Acid
    - H⁺ donor
    - $\text{HCl} + \text{H}_2\text{O} \rightarrow \text{H}_3\text{O}^+ + \text{Cl}^-$
    - HCl donates a proton to H₂O
  - Base
    - H⁺ acceptor
    - $\text{NH}_3 + \text{H}_2\text{O} \rightarrow \text{NH}_4^+ + \text{HO}^-$
    - NH₃ accepts a proton from H₂O
- Works for water and nonaqueous solvents
- Does not describe aprotic acids well
Lewis Acid-Base Theory

• Focused on electrons (e⁻)
  – Acid
    • e⁻ acceptor
    • HCl + H₂O → H₃O⁺ + Cl⁻
    • H⁺ accepts an e⁻ pair from H₂O
  – Base
    • e⁻ donor
    • :NH₃ + H₂O → NH₄⁺ + HO⁻
    • NH₃ donates an electron pair to H⁺
    • Works for all solvents

• Describes protic and aprotic acids
  – H⁺ is a Lewis acid
Acid-Base Strength

• $pK_a$
  – Describes acid strength
  – Larger number, weaker acid
    • Positive and negative numbers
    • $pK_a = -\log K_a$
    • $K_a = \frac{[A^-][H^+]}{[HA]}$

• Solvent dependent
  – Leveling effect in water and other amphiprotic solvents (all strong acids become $H_3O^+$, all strong bases become $OH^-$)
  – pH is related to but not equal to $pK_a$

• Describes protic and aprotic acids
  – $H^+$ is a Lewis acid
Brønsted Acid-Base Strength

<table>
<thead>
<tr>
<th>Acid Base</th>
<th>Value</th>
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<tbody>
<tr>
<td>CF₃SO₃H (TfOH)</td>
<td>-15</td>
</tr>
<tr>
<td>HCl</td>
<td>-8</td>
</tr>
<tr>
<td>H₃O⁺</td>
<td>-1.7 (0)aq</td>
</tr>
<tr>
<td>CH₃CO₂H (AcOH)</td>
<td>4.6</td>
</tr>
<tr>
<td>CH₃CH₂OH (EtOH)</td>
<td>16</td>
</tr>
<tr>
<td>(CH₃)₃COH (tBuOH)</td>
<td>18</td>
</tr>
<tr>
<td>NH₃</td>
<td>36</td>
</tr>
<tr>
<td>iPr₂NH</td>
<td>36</td>
</tr>
<tr>
<td>CH₃COCH₂COCH₃ (acac)</td>
<td>9</td>
</tr>
<tr>
<td>CH₃COCH₃ (acetone)</td>
<td>19</td>
</tr>
<tr>
<td>CH₃CO₂CH₂CH₃ (EtOAc)</td>
<td>24</td>
</tr>
<tr>
<td>HC=CH</td>
<td>26</td>
</tr>
<tr>
<td>CH₂=CH₃</td>
<td>45</td>
</tr>
<tr>
<td>CH₃CH₃</td>
<td>62</td>
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<tr>
<td></td>
<td>43</td>
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<tr>
<td></td>
<td>41</td>
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<tr>
<td>Substrate</td>
<td>pKa</td>
</tr>
<tr>
<td>-----------</td>
<td>-----</td>
</tr>
<tr>
<td>H2O</td>
<td>15.7</td>
</tr>
<tr>
<td>H3O+</td>
<td>-1.7</td>
</tr>
<tr>
<td>H2S</td>
<td>7.00</td>
</tr>
<tr>
<td>HBr</td>
<td>-9.00</td>
</tr>
<tr>
<td>HCl</td>
<td>-8.0</td>
</tr>
<tr>
<td>HF</td>
<td>3.17</td>
</tr>
<tr>
<td>HOCl</td>
<td>7.5</td>
</tr>
<tr>
<td>HClO4</td>
<td>-10</td>
</tr>
<tr>
<td>HCN</td>
<td>9.4</td>
</tr>
<tr>
<td>HN3</td>
<td>4.72</td>
</tr>
<tr>
<td>HSCN</td>
<td>4.00</td>
</tr>
<tr>
<td>H2SO3</td>
<td>1.9, 7.21</td>
</tr>
<tr>
<td>H2SO4</td>
<td>-3.0, 1.99</td>
</tr>
<tr>
<td>H3PO4</td>
<td>2.12, 7.21, 12.32</td>
</tr>
<tr>
<td>HNO3</td>
<td>-1.3</td>
</tr>
<tr>
<td>HNO2</td>
<td>3.29</td>
</tr>
<tr>
<td>H2CrO4</td>
<td>-0.98, 6.50</td>
</tr>
<tr>
<td>CH3SO3H</td>
<td>-2.6</td>
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<tr>
<td>CF3SO3H</td>
<td>-14</td>
</tr>
<tr>
<td>NH4Cl</td>
<td>9.24</td>
</tr>
<tr>
<td>B(OH)3</td>
<td>9.23</td>
</tr>
<tr>
<td>HOOH</td>
<td>11.6</td>
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<tbody>
<tr>
<td>OH</td>
<td>15.7</td>
<td>(31.2)</td>
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<tr>
<td>MeOH</td>
<td>15.5</td>
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</tr>
<tr>
<td>iPrOH</td>
<td>16.5</td>
<td>(29.3)</td>
</tr>
<tr>
<td>iBuOH</td>
<td>17.0</td>
<td>(29.4)</td>
</tr>
<tr>
<td>CH3CN</td>
<td>24.0</td>
<td></td>
</tr>
<tr>
<td>CF3CH2OH</td>
<td>12.5</td>
<td>(23.5)</td>
</tr>
<tr>
<td>(CF3)2CHOH</td>
<td>9.3</td>
<td>(18.2)</td>
</tr>
<tr>
<td>C6H5OH</td>
<td>9.95</td>
<td>(18.0)</td>
</tr>
<tr>
<td>m-O2NC6H4OH</td>
<td>8.4</td>
<td></td>
</tr>
<tr>
<td>p-O2NC6H4OH</td>
<td>7.1</td>
<td>(10.8)</td>
</tr>
<tr>
<td>p-OMeC6H4OH</td>
<td>10.2</td>
<td>(19.1)</td>
</tr>
<tr>
<td>2-naphtol</td>
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| Values <0 for H2O and DMSO, and values >14 for water and >35 for DMSO were extrapolated using various methods.

For a comprehensive compilation of Bordwell pKa data see: [http://www.chem.wisc.edu/areas/reich/pkatable/index.htm](http://www.chem.wisc.edu/areas/reich/pkatable/index.htm)

Lewis Acids and Bases

• Acids
  – Trigonal AlX$_3$/BX$_3$
    • R = X, H, alkyl
    • Deficiency at Al/B
  – Tetrahedral TiX$_4$

• Bases
  – Amines/Phosphines
  – Alcohols/Ethers/S
  – Carbonyls/S
  – Alkenes/Arenes
Hard and Soft Acids and Bases

- **Hard Acid/Base**
  - Charge is localized
  - Compact
  - $\text{Al}^{3+}$ is harder than $\text{In}^{3+}$

- **Soft Acid/Base**
  - Charge is delocalized
  - Diffuse
  - $\text{I}^-$ is softer than $\text{F}^-$
  - $\text{CH}_3\text{Cu}$ is softer than $\text{CH}_3\text{Li}$
  - Multiple bonds are generally soft as compared to lone pairs
    - Atom-depend

Hard acids react with hard bases
  - $\text{AlCl}_3 + \text{Cl}^- \rightarrow \text{AlCl}_4^-$

Soft acids react with soft bases

Principle of “Maximum Hardness”

$$\text{HCl} + \text{H}_2\text{O} \quad \rightarrow \quad \text{H}_3\text{O}^+ + \text{Cl}^-$$

$$\text{AcOH} + \quad \text{H}_2\text{O} \quad \leftarrow \quad \text{H}_3\text{O}^+ + \text{AcO}^-$$

$$\text{Hg}_2\text{Cl}_2 + \text{H}_2\text{S} \quad \rightarrow \quad \text{HCl} + \text{HgS}$$

Carey and Sundberg  Part A pp 16-18
Hard and Soft Acids and Bases

• Catalytic hydrogenation

\[
\begin{align*}
\text{CH}_2 \text{CH}_2 + \text{PdH}_2 & \leftrightarrow \text{CH}_2 \text{CH}_2 \text{PdH}_2 & \text{H}_2 \\
\text{CH}_3 \text{CH}_3 + \text{Pd} & \leftrightarrow \text{H}_2 \text{C-Pd} & \text{CH}_3 \\
\end{align*}
\]

• Hydroboration

\[
\begin{align*}
\text{CH}_2 \text{CH}_2 + \text{BH}_3 & \leftrightarrow \text{CH}_2 \text{CH}_2 \text{BH}_3 & \text{H}_2 \text{C--BH}_2 \\
\text{H}_2 \text{C--BH}_2 & \rightarrow \text{CH}_3 & \text{H}_2 \text{C--BH}_2 \\
\end{align*}
\]
Reactive Carbon Intermediates

- **Carbocations (acids)**
  - Trigonal (sp)
  - Free
  - Ion-paired
- **Carbanions (bases)**
  - Free
  - Ion-Paired
- **Radicals (neither/both)**
  - Uncharged
  - Electron deficient
- **Carbenes**
  - Paired
  - Unpaired (biradical)
Reactive Carbon Intermediates

- Carbanions (bases)
  - May be tetrahedral, trigonal, or digonal (linear)
  - Free or Ion-Paired
  - Stability depends on R
    - e- withdrawing groups
    - \(\pi\) systems
  - Reacts with electrophiles/oxidizing agents
    - Carbonyls/imines
    - Electron deficient alkenes
    - Alkyl halides (depends on metal)
    - Oxygen/peroxides

Carey, Section 14.5; Carey and Sundberg Part A 3.4.2, Part B 10.1
Reactive Carbon Intermediates

• Carbocations (carbonium ions)
  – Mostly Trigonal (sp$^2$)
  – Lewis Acids
  – Free or Ion-paired
  – Stability depends on R
    • e- donors
    • π systems
  – Rearrange to most stable
    • 1,2-shifts (H, alkyl, aryl)
    • π systems
  – React with nucleophiles
    • Anions
    • Alkenes/arenes
    • Certain hydrides (eg Et$_3$SiH)

Carey, Section 4.10, 10.3, 11.14;
Carey and Sundberg  Part A 3.4.1 Part B, Section 10.1
Reactive Carbon Intermediates

• Radicals (neither/both)
  – Uncharged
  – Electron deficient
  – Stabilized by both electron donors and acceptors
  – Can be electrophilic or nucleophilic depending on substitution

• Carbenes
  – Paired
  – Unpaired (biradical)
  – May be free or bound (carbenoids)

Carey, Section 4.10, 10.3, 11.14;
Carey and Sundberg  Part A 3.4.1 Part B, Section 10.3
Writing Reaction Mechanisms

• What species is involved (cation, anion, radical)?
• Where are there excess electrons?
• Where is there an electron deficiency?
• What are the conditions?
  – Don’t neglect the character of the solvent
    • Polar, nonpolar, ethers, esters, amides, additives (HMPA)
  – Generally no anionic intermediates in acid
  – Generally no cationic intermediates in base
  – Is heat or light involved (radicals)

www.abdn.ac.uk/curly-arrows/
http://chemistry.umeche.maine.edu/CHY252/Mechan.html
Writing Reaction Mechanisms

• Virtually every mechanistic step is an acid-base reaction.
• Every step is balanced to atoms, electrons and charges.
• Generally, no more than four bonds are broken/formed (except pericyclic reactions).
• Generally, no more than two entities involved.
• All intermediates must be plausible.

www.abdn.ac.uk/curly-arrows/
http://chemistry.umeche.maine.edu/CHY252/Mechan.html
Writing Reaction Mechanisms

• Use curved arrows to indicate electron flow.
  – Double barbed for 2 electrons
  – Single barbed for 1 electron (radicals)
• Show the moving electrons explicitly
  – Draw lone pairs if relevant
  – Arrow begins at lone pair, radical center or bond
  – Arrow ends at the atom where the electron(s) are forming the new lone pair, radical center or bond.
• Only one set of electrons move at a time unless it is a concerted reaction.
• Electrons don’t attack other electrons

www.abdn.ac.uk/curly-arrows/
http://chemistry.umeche.maine.edu/CHY252/Mechan.html
Basic Mechanistic Steps

• Each step should be labeled as to what is occurring

• Primary process types
  – Nucleophile In – a bond is being made between cationic and anionic centers
  – Nucleophile Out – a bond is being broken producing a cation and anion
  – Proton Transfer

• Other types
  – Sigmatropic rearrangements and pericyclic [m,n]
  – Radical abstractions/rearrangements
  – Metal mediated steps
    • Oxidative addition/reductive elimination
Implausible intermediates/processes

- Hypo/hypervalent atoms (esp. 1\textsuperscript{st} row)
  - No more than 8e-, no less than 6e-
- Dianions, dications, or diradicals
  - Except in well recognized cases
  - A very strong base is required to doubly deprotonate
- Cation and anion on the same molecule
  - Except ylides and some conjugated dipoles

www.abdn.ac.uk/curly-arrows/
http://chemistry.umeche.maine.edu/CHY252/Mechan.html
Implausible intermediates/processes

• Intramolecular is faster than intermolecular
  – As long as similar energetics are involved
  – $S_N1$ vs E1

• Nucleophilic attack at congested centers
  – $S_N2$ at tertiary center

• Reactions that only happen in mass spectrometers and atom smashers
  – (unless you are working on a mechanism for a mass spectrometer or atom smasher)

www.abdn.ac.uk/curly-arrows/
http://chemistry.umeche.maine.edu/CHY252/Mechan.html
Mechanisms: The S_N1 reaction

First, this reaction is incomplete. A proper reaction includes all reactants and products.

Now, consider where the electrons are and the relative strength of nucleophile and electrophile

These won't react with each other as is, so something must happen first (first order kinetics in tBuBr).
Mechanisms: The \( S_N 1 \) reaction

Overall Reaction

Each individual step is an acid-base reaction.
Mechanisms: The $S_N1$ reaction

Overall Reaction

In the end, cancel everything that is duplicated on both sides of the reaction arrow, leaving the elements of the overall reaction equation.