Design at the Molecular Level

“All rules of thumb are half-truths... some are useful.”

Marty Mulvihill, Class 13, Monday March 7th

Definitions

1. **Degradation**: Breakdown of chemicals, through physical, chemical or biological pathways
2. **Biodegradation**: Breakdown of chemicals by living organisms
3. **Readily Biodegradable**: At least 60-70% of the material must be broken down within ten days
4. **Mineralization**: Complete conversion of chemical substances into their simplest naturally occurring fragments (Usually CO₂ and H₂O)
5. **Recalcitrance**: Resistant to biological action
6. **Oxidation**: Adding ‘O’ to the chemical structure
7. **Hydrolysis**: Fragmentation by the addition of water
8. **Esterase**: Enzyme that catalyzes Hydrolysis
9. Any other terms from the reading?
Outline

1. Chemical Cycles
2. Small Molecule Design Rules
3. Polymer Design Rules
4. What about toxicity?
Modification of Chemical Cycles

- Increase Production
- Increase Population
- Rate of production larger than rate of degradation
- Move towards closed loop systems.
- Development w/o growth

Pathways for chemical degradation

Pathways:
- Combustion
- Photolysis
- Hydrorolysis
- Biodegradation
  - Aerobic
  - Anaerobic

Factors:
- Environmental Compartment
- Absorption Cross-section
Humans closing the loop

Incineration-Combustion Pathway
• One hundred tons of town refuse is equal to 30 tons of coal in fuel value
• Problems with halogenated compounds

Recycling- Engineering new cycles
• About 3% of plastic is currently recycled
• At present the cost of recovery limits recycling activities.
• EU targets to recover 50–65% and recycle 25–45% of all packaging waste

Creating more degradable chemical products

Small Molecules in Society
• Global Chemical Manufacturing = $3 trillion
• US largest producer of chemicals in the world $664 billion.
• American chemistry creates 2% of the US GDP.
Design for Degradation

Help Degradation:
• Esters
• Oxygen (except ethers)
• Unsubstituted Linear alkyl chains

Hinder Degradation:
• **halogens**, especially chlorine and fluorine and especially if there are more than three in a small molecule (iodine and (probably) bromine contribute to a lesser extent);
• **chain branching** if extensive (quaternary C is especially problematic);
• **Nitrogen**: tertiary amine, nitro, nitroso, azo, and arylamino groups;
• **polycyclic residues** (such as in polycyclic aromatic hydrocarbons), especially with more than three fused rings;
• **heterocyclic residues**, for example, imidazole;
• **aliphatic ether bonds** (except in ethoxylates)

What we don’t want: Persistent Organic Pollutants (POPs)
Example: Dielectric Coolants (and pump oil...)

Replacing:

Example: Soap
Example: Biocides

Modeling and Other Resources

• **EPA Estimation Program Interface (EPI) Suite**
  - All free and available online.
  - Automates the rules of thumb in an additive fashion.

• **CleanGredients**
  - Not freely available ($150/yr non-profit)

• **University of Minnesota Biocatalysis/Biodegradation database.**
  - Shows detailed pathways with enzymes identified.
Plastics in Society

• The annual growth rate of the use of plastics in packaging is approximately 25%.

• Polymers are estimated to be approximately 20% of the volume of municipal solid waste.

• 15 million tons of polyethylene produced in 2000.

Polymer Design Rules

Promote Degradation
• Hydrophilicity
• Hydrolysable linkages such as amide, esters, urea, and urethanes groups.
• Biological feedstocks
• Include chromophores

Hinder Degradation
• Branching
• Highly substituted polymers
• Halogens
Common Biodegradable Polymers

Poly alcohols

Starches

Esters

PHB/V

PLA

PCL

Starch: Balance between functions

- Derivitization at the -OH is needed to increase processibility, function and compatibility.
  - Acetylation reaction using an active chloride or anhydride in a pyridine solvent
  - Green Alternative: acetylation of starch in 3% aqueous sodium hydroxide and at pH 8
- Best plasticity occurs with ~1.5 substitutions/monomer
- Increasing substitution, decreases biodegrability.
Esters: The polymer du jour

- PHB & PLA are fermentation products.
- Degradation in sea water: PCL > PHB > PLA
- Polyesters can be depolymerized to give monomer.
- Polyesters disrupt the recycling of polyethylene

### Green Chemistry and LCA for Polymers

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Rank by GC Principles</th>
<th>Rank by LCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLA (NatureWorks)</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>PHA (Utilizing Stover)</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>PHA (General)</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>PLA (General)</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>High Density Polyethylene</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Polyethylene Terephthalate</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Low Density Polyethylene</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Bio-polyethylene Terephthalate</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Polypropylene</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>General Purpose Polystyrene</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Polyvinyl Chloride</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Polycarbonate</td>
<td>12</td>
<td>11</td>
</tr>
</tbody>
</table>

Beckman et al, EST, 2010, 8264.
Poly vinyl alcohol

- Elmer’s Glue
- Petroleum feedstock
- Prepared from vinyl acetate, followed by hydrolysis
- Compatible with polyethylene in blends.
- Can be used with starch to make biodegradable packaging

Blends: The best of both worlds?

For biodegradation:
Polyethylene blends with

For Photolysis:
Add metal salts or other chromophores
The hard work of predicting toxicity


Oxidation is one of the first ways that biology interacts with chemicals.
Mechanism Matters

Molecular Design considerations

1. Reduce Bioavailability
2. Increase excretion/reduce storage
3. Reduce rate of distribution
4. Reduce rate of toxicodynamic interaction or potency of toxicophore

Lipinski rules
- poor absorption is likely when
  - $\log P_{ow} > 5$
  - Mol. Wt. > 500 g/mol
  - > 5 H-bond donors
  - > 10 H-bond acceptors (sum all N’s and O’s)
- Substrates for biological transporters are exceptions to the rule
Biodegradability vs. Hazard reduction

<table>
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<tr>
<th>structural modification</th>
<th>toxicity end point/objective</th>
<th>effect on biodegradability</th>
</tr>
</thead>
<tbody>
<tr>
<td>increase MW to &gt;1000</td>
<td>lower aquatic toxicity</td>
<td>decrease</td>
</tr>
<tr>
<td>reduce water solubility to &lt;1 μg/L</td>
<td>lower aquatic toxicity</td>
<td>decreases availability to biodegradation enzymes</td>
</tr>
<tr>
<td>increase steric hindrance at active site</td>
<td>lower aquatic toxicity</td>
<td>decreases availability to biodegradation enzymes</td>
</tr>
<tr>
<td>add bulky ortho groups</td>
<td>reduce oncogenicity concern for aromatic amines</td>
<td>decreases accessibility to biodegradation enzymes</td>
</tr>
<tr>
<td>add hydrophilic groups (sulfonate or COOH)</td>
<td>reduce oncogenicity concern (enhance excretion)</td>
<td>may increase or decrease depending on group</td>
</tr>
</tbody>
</table>

Returning to PFC’s

1. Could you design a better PFC?
2. Which do you like better Polymer or surfactant PFC’s? Why?
Molecular Design

What will you consider and why?

Feedstock $\rightarrow$ Reagents $\rightarrow$ Final properties

12 Principles of Green Chemistry

1. Prevent waste
2. Atom economy
3. Less hazardous chemical synthesis
4. Design safer chemicals
5. Safer solvents/reaction media
6. Energy efficiency
7. Use renewable feedstocks
8. Reduce derivatives
9. Catalysis
10. Design for end of life
11. Real-time process control
12. Inherently safer chemistry

How does this shape the interpretation or execution of the 12 principles?