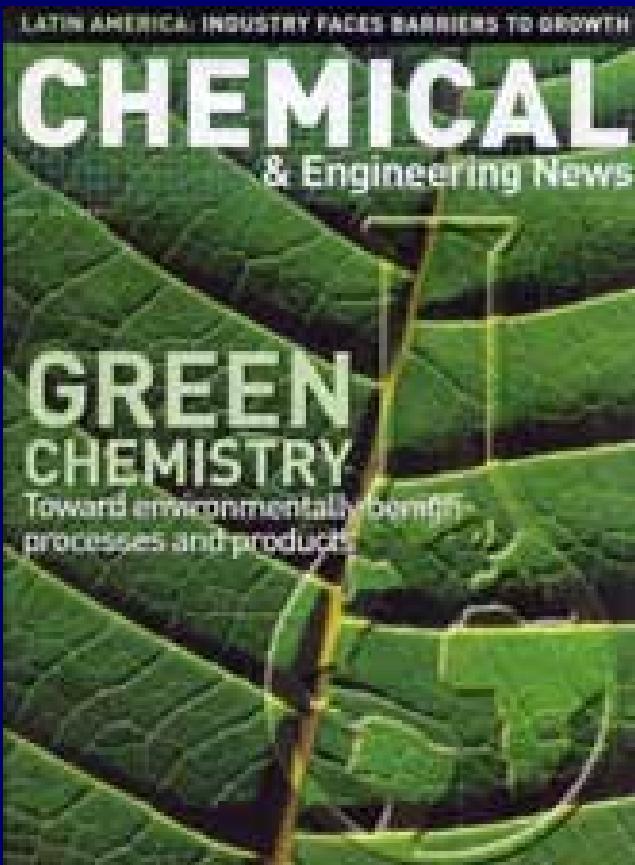


Green Chemistry: Principles and Practice

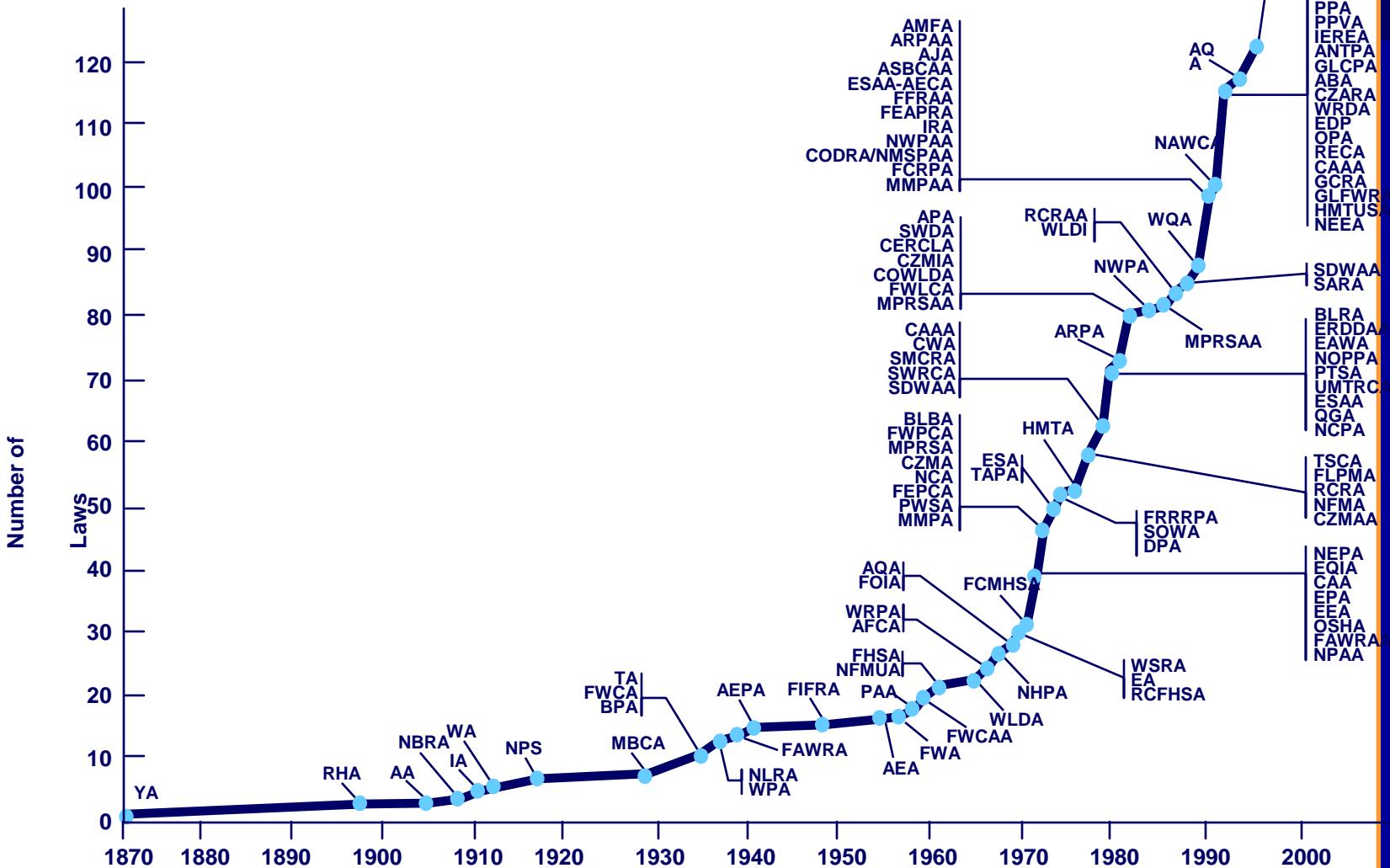
Mary M. Kirchhoff
Summer School on Green Chemistry
and Sustainable Energy
23 July 2013

What Is Green Chemistry?



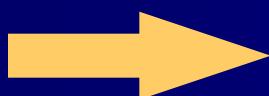
- Green chemistry is the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances.

Growth in U.S. Environmental Regulations



Pollution Prevention Act of 1990

Pollution
Prevention

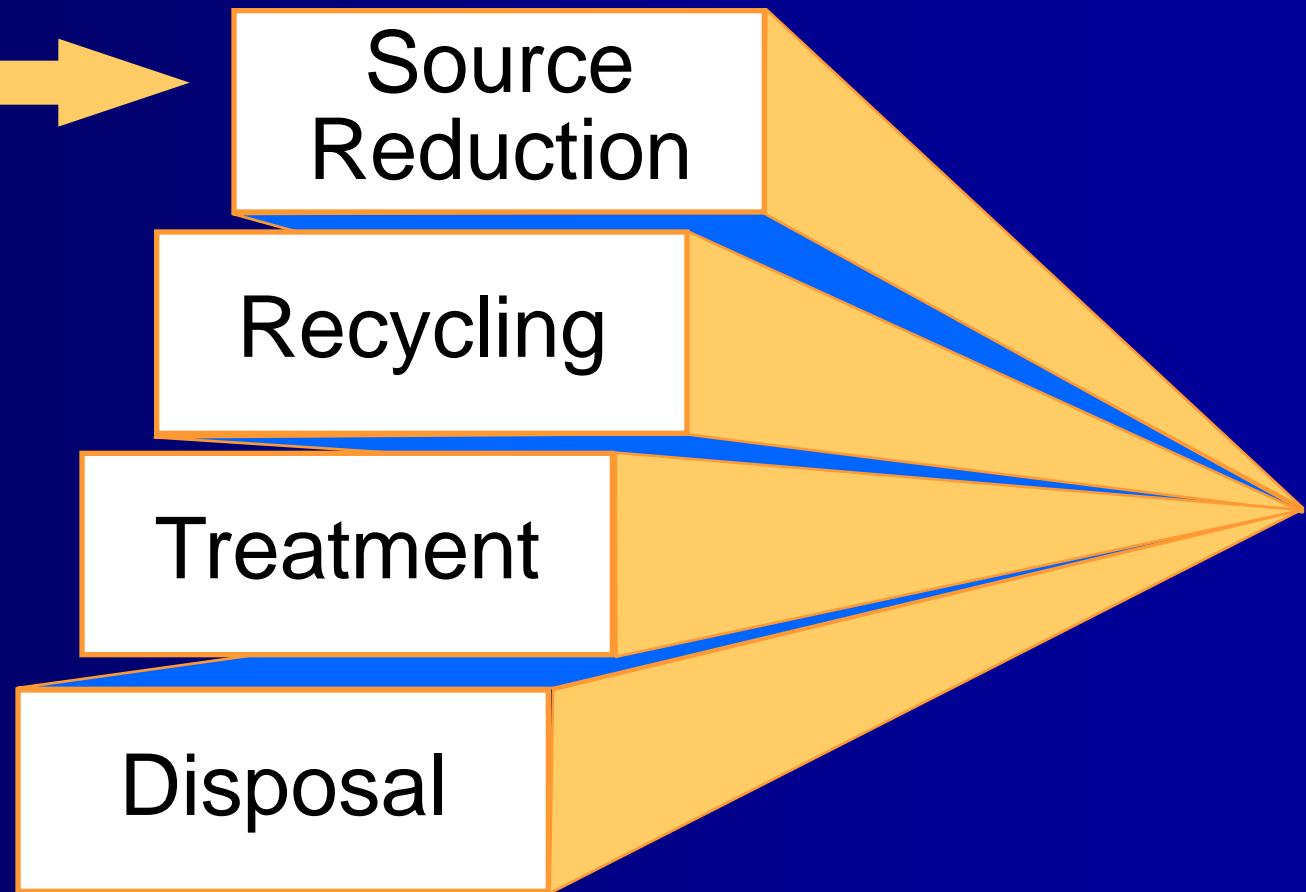


Source
Reduction

Recycling

Treatment

Disposal



12 Principles

- 1. Prevention
- 2. Atom Economy
- 3. Less Hazardous Chemical Syntheses
- 4. Designing Safer Chemicals
- 5. Safer Solvents and Auxiliaries
- 6. Design for Energy Efficiency
- 7. Use of Renewable Feedstocks
- 8. Reduce Derivatives
- 9. Catalysis
- 10. Design for Degradation
- 11. Real-time Analysis for Pollution Prevention
- 12. Inherently Safer Chemistry for Accident Prevention

Presidential Green Chemistry Challenge

- The Presidential Green Chemistry Challenge was established to *recognize* and *promote* fundamental and innovative chemical technologies that accomplish pollution prevention through source reduction and that are useful to industry.



Principle 1

It is better to prevent waste
than to treat or clean up
waste after it is formed.

E-factor

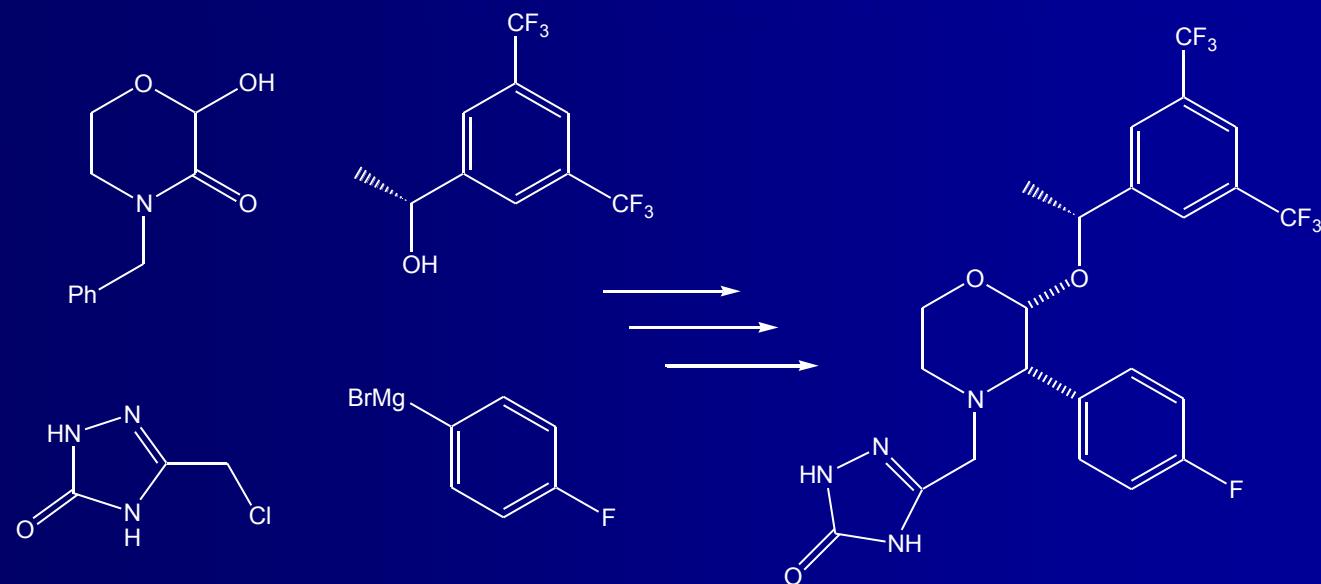
■ Weight of byproducts/weight of desired product	
– Oil refining	0.1
– Bulk chemicals	<15
– Fine chemicals	5-50
– Pharmaceuticals	25-100+

Sheldon, *Chem Tech*, 1994, 24, 38.

Aprepitant Synthesis

- ◆ Doubles yield
- ◆ Eliminates 340,000 L of waste/ton product

Merck



Aprepitant Statistics

- 85% reduction in raw materials use
- 80% reduction in water usage
- 85% reduction in waste
- 75% lower manufacturing costs
- E-factor
 - Reduced from 477 to 66

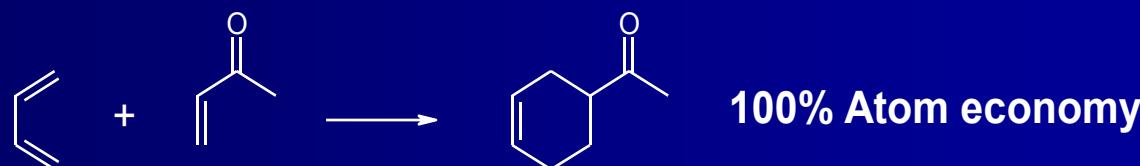
Principle 2

Synthetic methods should be designed to maximize the incorporation of all materials used into the final product.

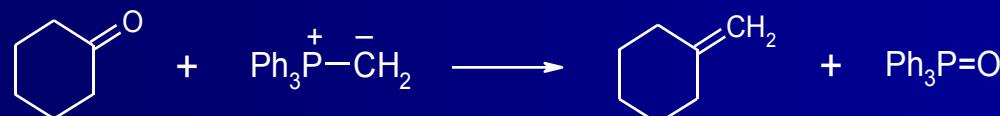
Atom Economy

$$\text{Atom economy} = \frac{\text{MW of desired product}}{\text{Sum of MWs of all substances produced}}$$

Diels-Alder Reaction

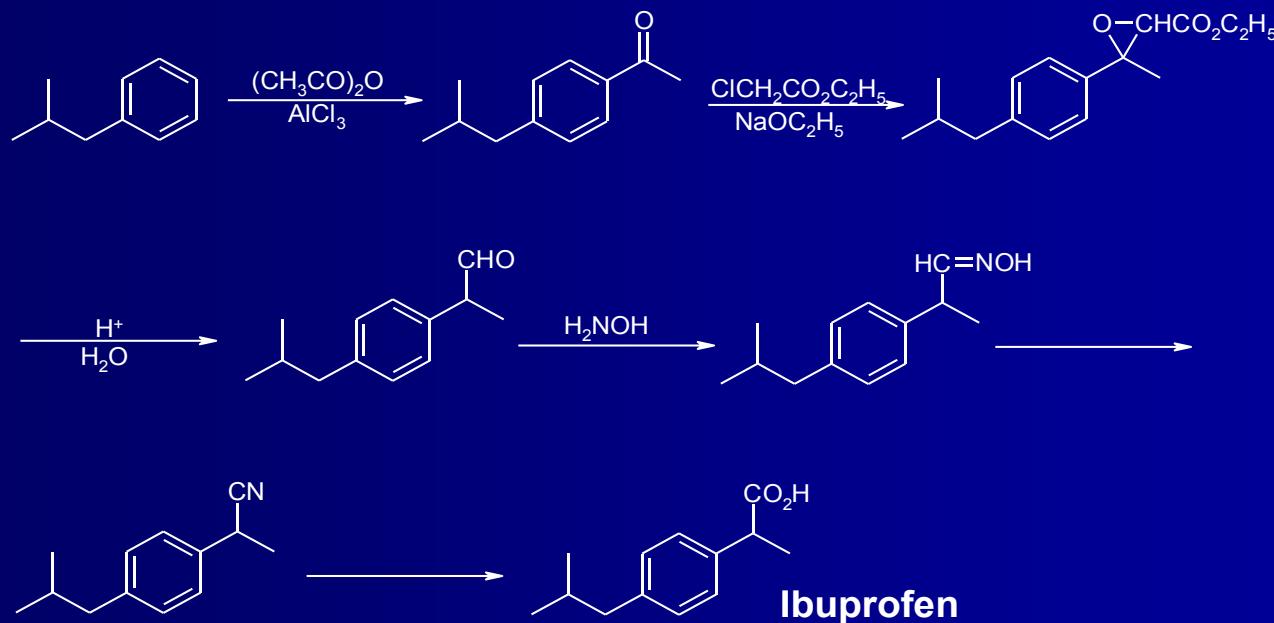


Wittig Reaction



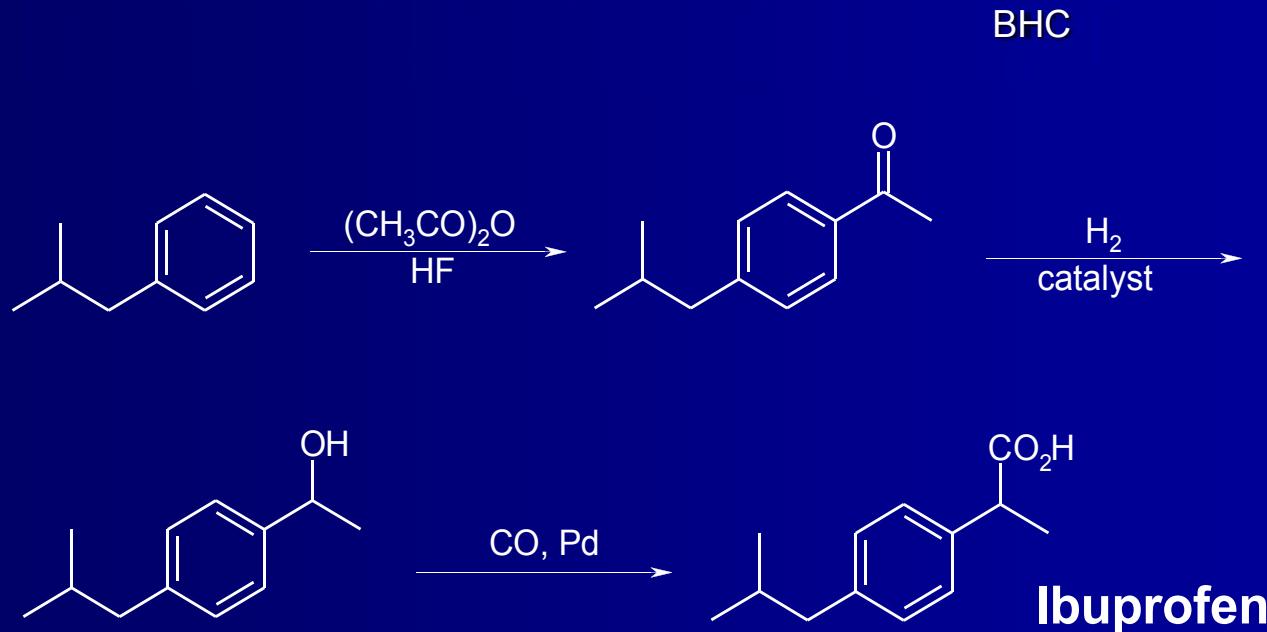
Atom Economy

- Traditional synthesis of ibuprofen
 - 6 stoichiometric steps
 - <40% atom utilization



Atom Economy

- Catalytic synthesis of ibuprofen
 - 3 catalytic steps
 - 80% atom utilization (99% with recovered acetic acid)



Principle 3

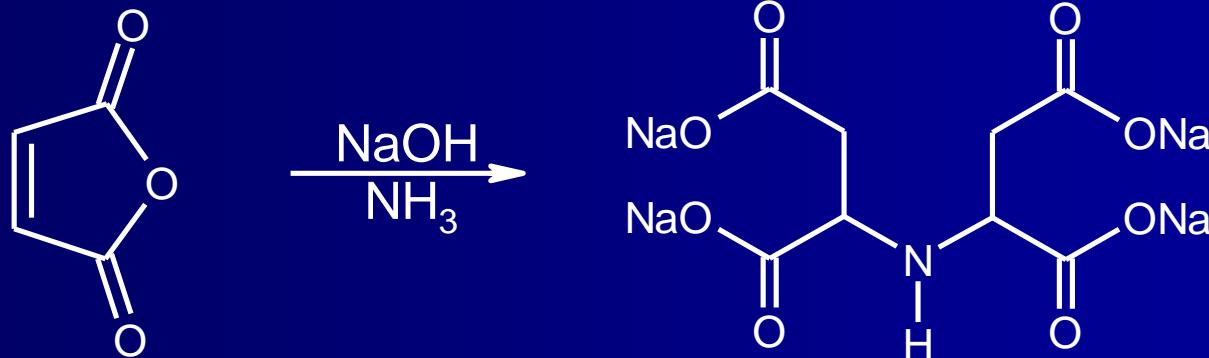
Wherever practicable,
synthetic methodologies
should be designed to use
and generate substances
that possess little or no
toxicity to human health and
the environment.

Alternative Reaction Conditions

◆ Sodium iminodisuccinate

- Biodegradable, environmentally friendly chelating agent
- Synthesized in a waste-free process
- Eliminates use of hydrogen cyanide

Bayer Corporation and Bayer AG



Principle 4

Chemical products should be designed to preserve efficacy of function while reducing toxicity.

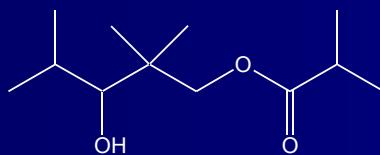
Safer Chemicals: Reduced VOC Paints

- Coalescent: added to paint to provide a smooth, continuous finish
- 120 billion lbs volatile coalescents lost to atmosphere in U.S. each year

Archer Daniels Midland



Archer RC propylene glycol monoester

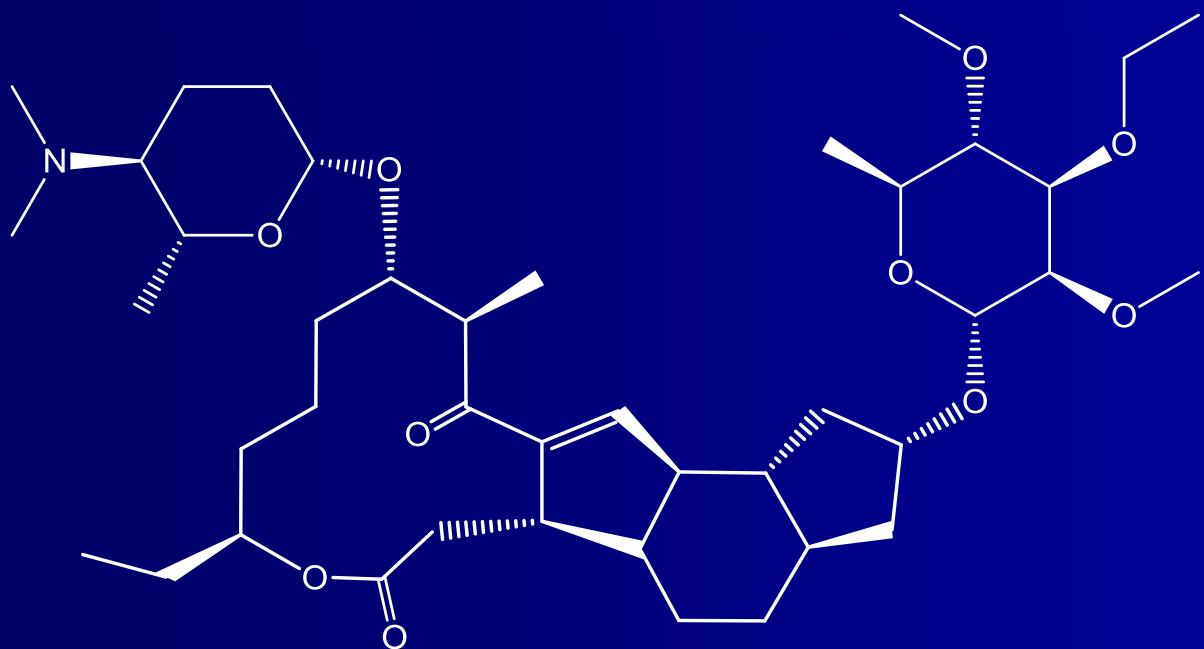


2, 2, 4-trimethyl-1, 3-pentanediol monoisobutyrate

Spinetoram

- Produced by fermentation of renewable feedstocks using *Saccharopolyspora spinosa*

Dow AgroSciences



Evolution of a Greener Technology

- 1999: Spinosad (Dow AgroSciences)
 - Selective, environmentally-friendly insecticide
- 2008: Spinetoram (Dow AgroSciences)
 - Controls wider range of pests at lower use rates than Spinosad
- 2010: Natular[®] Larvicide (Clarke)
 - Spinosad-based mosquito larvicide that slowly releases in water (Sequential Plaster Matrix)

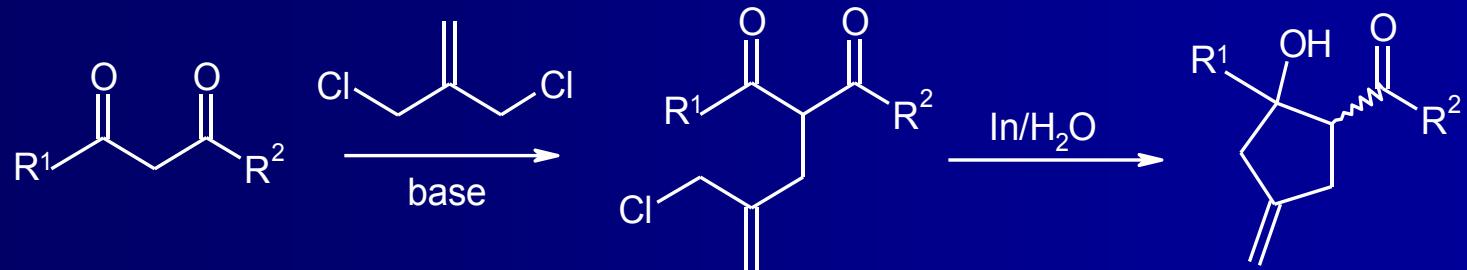
Principle 5

The use of auxiliary substances (e.g. solvents, separation agents, etc.) should be made unnecessary wherever possible and, innocuous when used.

Benign Solvents: H₂O

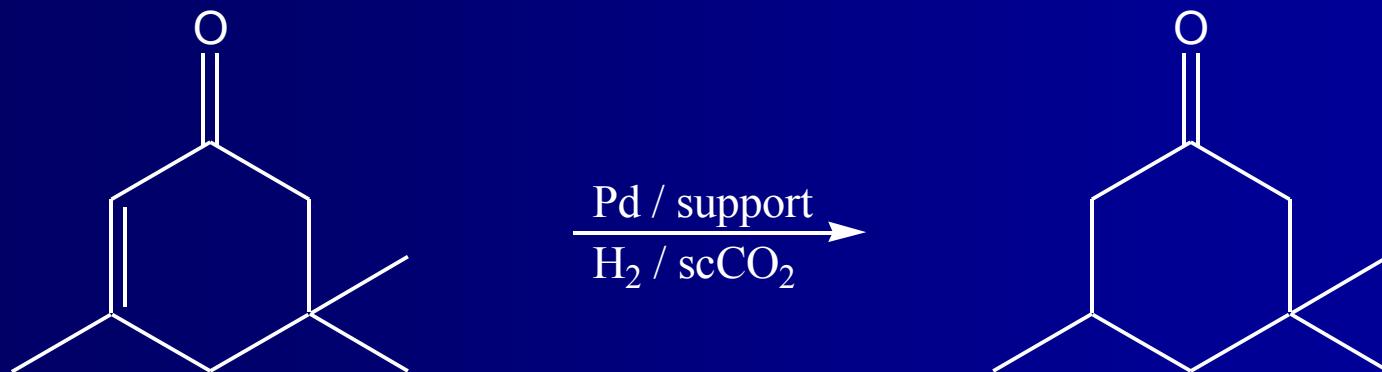
- Carbon-carbon bond formation in water
 - Diels-Alder, Barbier-Grignard
- Indium-mediated cyclopentanoid formation

Li, McGill University



Benign Solvents: CO₂

- Organic reactions in sc-CO₂
- Partnership between the University of Nottingham and the Thomas Swan & Company



Principle 6

Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.

MAX HT™ Bayer Sodalite Scale Inhibitor

- Bayer process: converts bauxite ore to alumina
- Problem: aluminosilicate crystals build up in heat exchangers/pipes
 - Decreases efficiency of heat exchange
 - Requires cleaning with H_2SO_4
- MAX HT™ inhibits crystal formation
- Annual savings per plant: \$2-20 M,
9.5-47.5 trillion BTU

Cytec

Principle 7

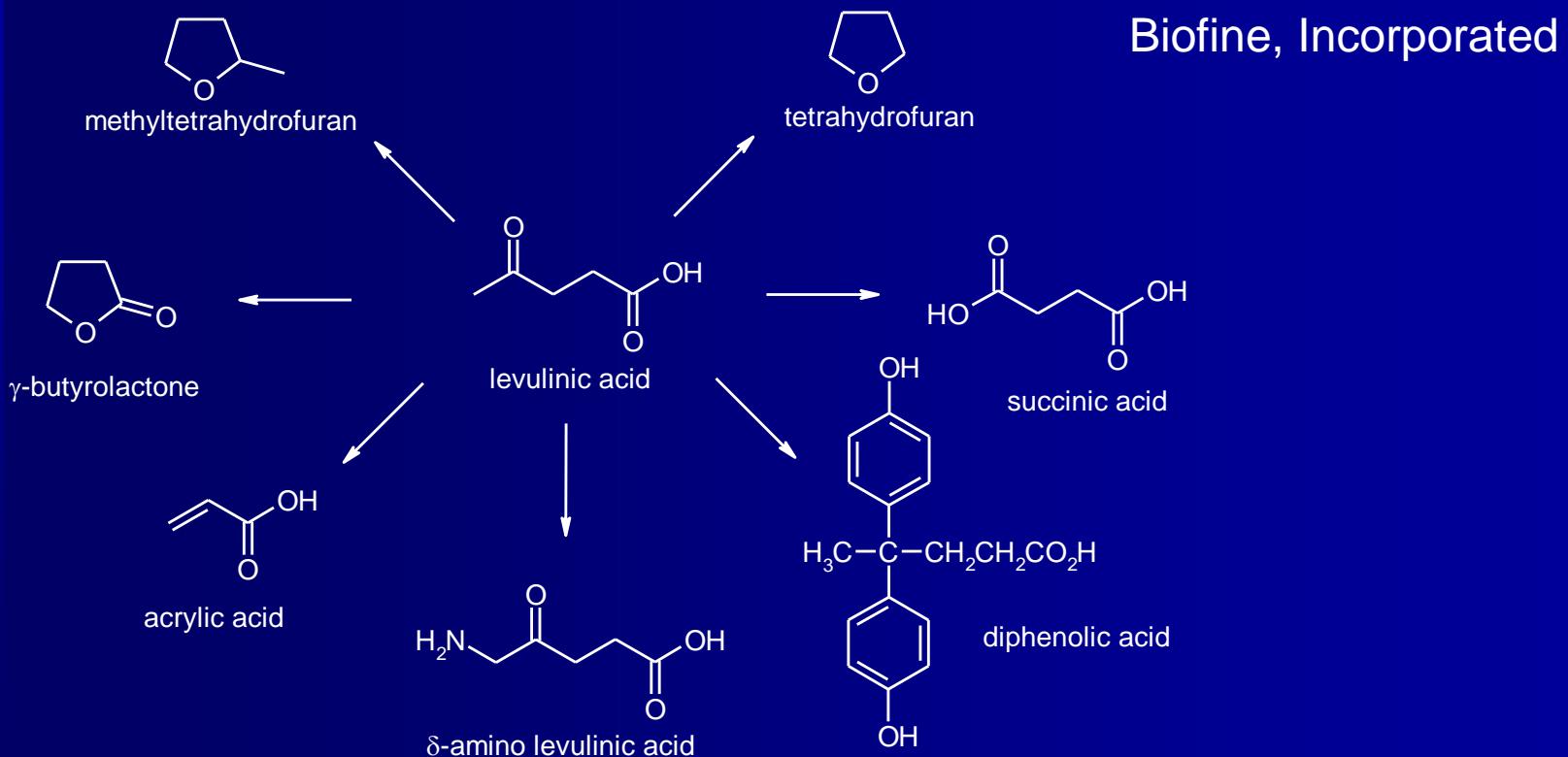
A raw material or feedstock should be renewable rather than depleting wherever technically and economically practicable.

Maximyze® Enzymes

- Cellulase enzymes produced by fermentation from renewable resources
- Improved paper strength
 - Reduces wood pulp needed
 - Increases use of recycled paper
 - Decreases energy use
 - Reduces use of chemicals added to improve paper strength

Renewable feedstocks

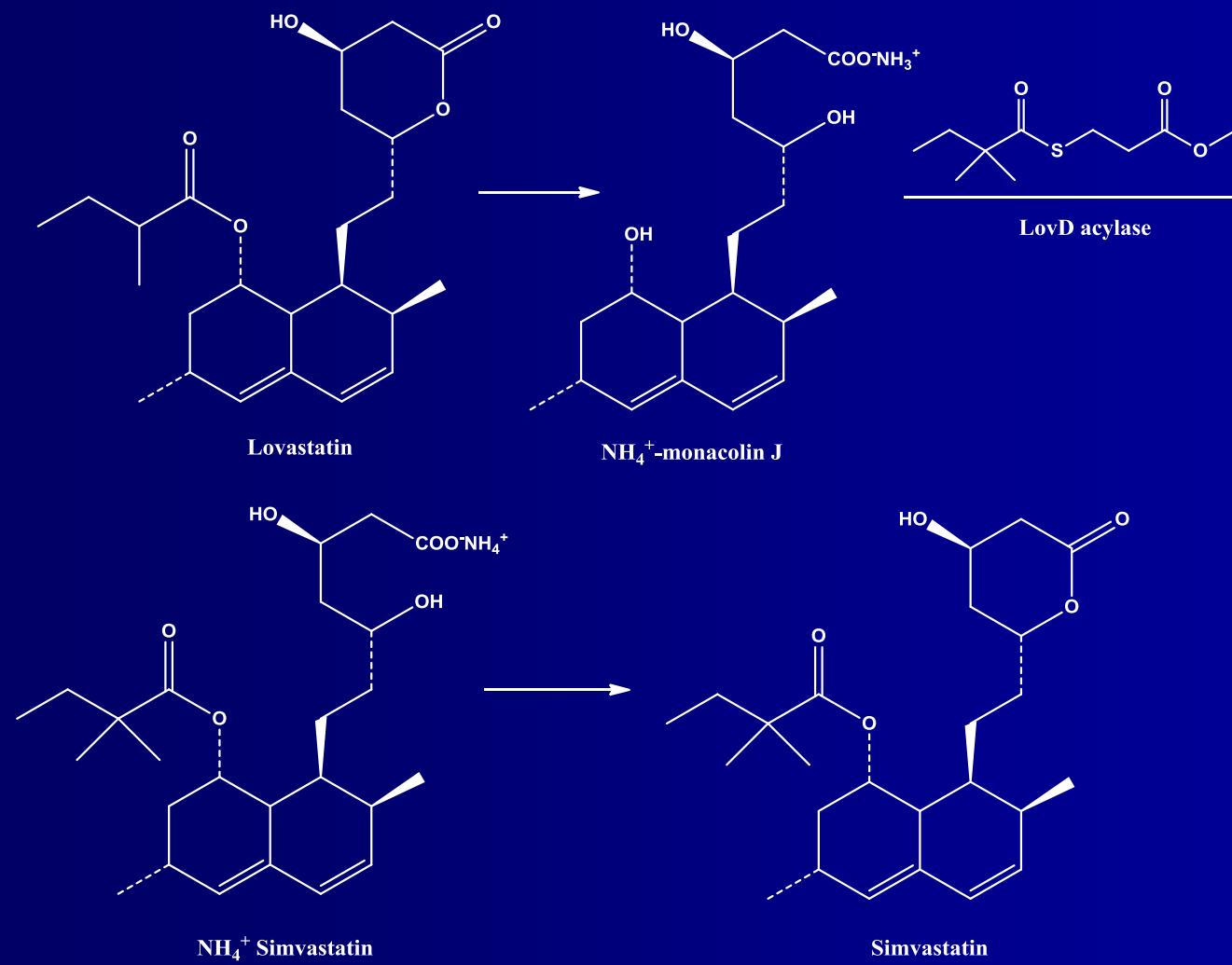
- ◆ Conversion of waste biomass to levulinic acid
 - paper mill sludge, municipal solid waste, unrecyclable waste paper, agricultural residues



Principle 8

Unnecessary derivatization
(blocking group,
protection/deprotection,
temporary modification of
physical/chemical
processes) should be
avoided whenever possible.

Synthesis of Simvastatin



Boric-Acid Mediated Amidation

- Direct amidation of carboxylic acids with amines
 - Boric acid: nontoxic, safe, inexpensive
 - Eliminates use of SOCl_2 , PCl_3 , phosgene
 - Widely applicable

Emisphere Technologies, Inc



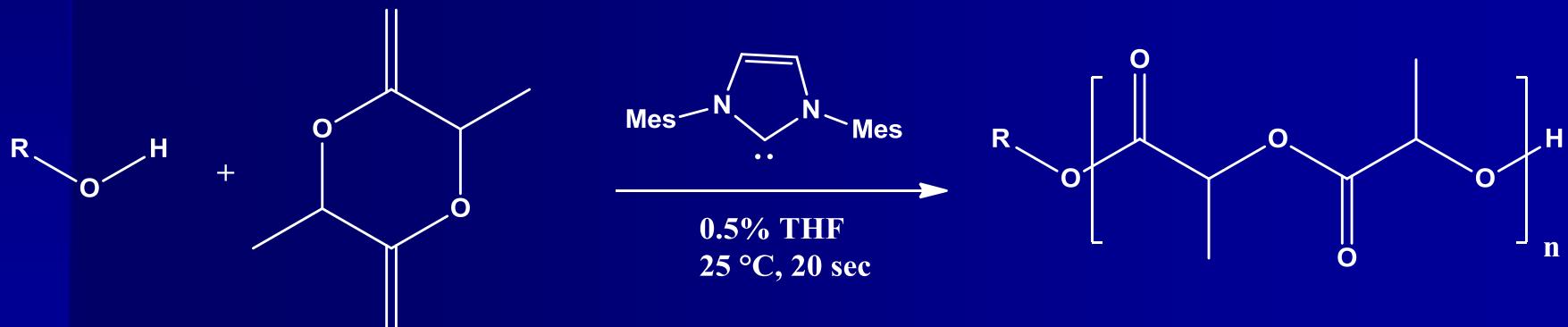
Principle 9

Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

Catalysis for Green Polymers

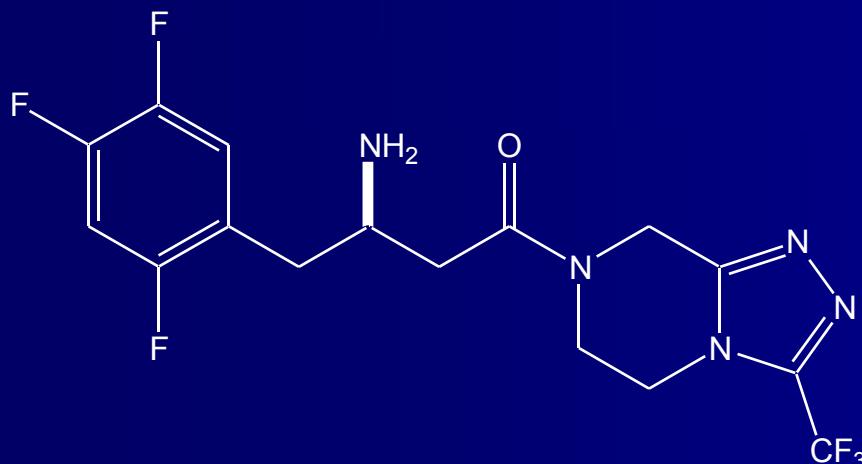
- Metal-free organic catalysts applied to the synthesis and recycling of polyesters

Waymouth & Hedrick



Greener Manufacture of Sitagliptin

- Sitagliptin, active ingredient in Januvia™
 - Treatment for Type II diabetes, controls blood sugar without significant side effects
 - Transaminase-based process with broad applications for converting ketones to chiral amines



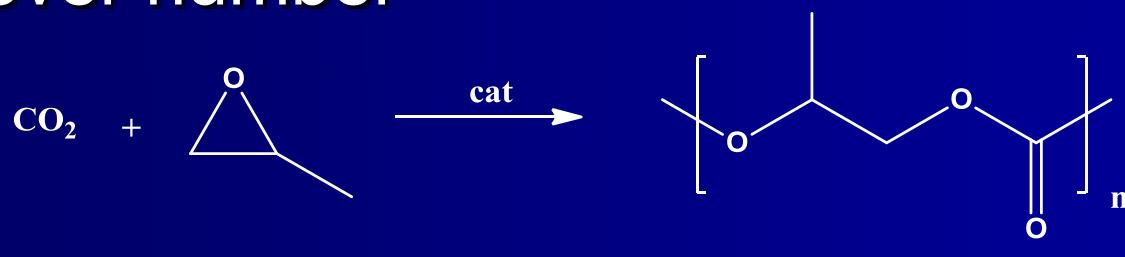
Merck & Codexis

Principle 10

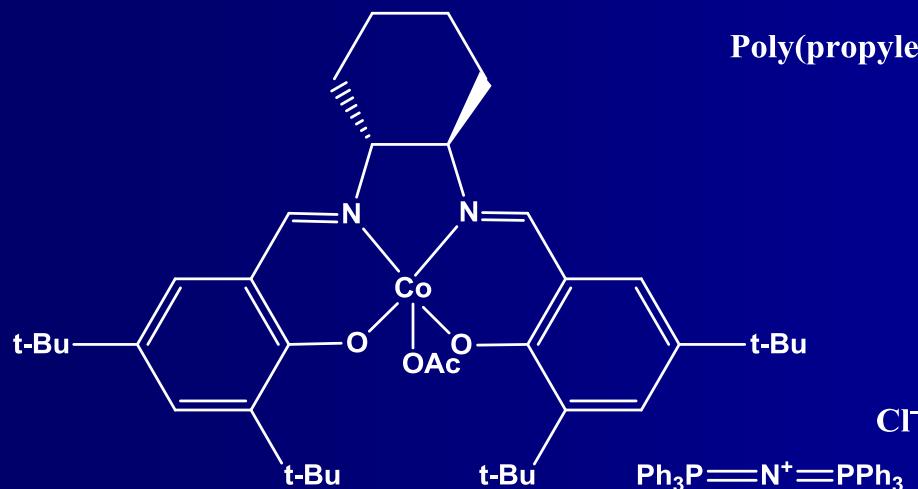
Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products.

Biodegradable Polymers

- CO and CO₂ used as monomers
- Catalyst exhibits high activity and high turnover number



Poly(propylene carbonate)



Cr⁻

Ph₃P=N⁺=PPh₃

Coates

Principle 11

Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.

Protein Testing

- Automated protein tagging technique
 - Tags amino acids commonly found in proteins
 - Employs non-toxic solutions
 - Generates no hazardous waste
 - Replaces hazardous materials and high temperatures in traditional methods
 - Applications in the food and pet food sectors

Principle 12

Substances and the form of a substance used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires.

2008 Small Business Winner

- Stabilized Alkali Metals
 - Alkali metals encapsulated in nanoscale porous metal oxides
- Increased safety, decreased storage and handling requirements
- Applications
 - Pharmaceutical/industrial
 - Processing water into hydrogen fuel
 - Remediation

Sustainable Development

- Development that meets the needs of the present without compromising the ability of future generations to meet their own needs.

Brundtland Commission

Green Chemistry and Sustainability

- Green chemistry is a tool in achieving sustainability
 - Not a solution to all environmental problems
 - Fundamental approach to pollution prevention
 - Chemistry's unique contribution to sustainability



Instructors

- Tamer Andrea
- Eric Beckman
- Joan Brennecke
- David Constable
- Ken Doxsee
- Nancy Jensen
- Mary Kirchhoff
- Corrie Kuniyoshi
- Mark Nimlos
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- Ryan Richards
- Kim Williams