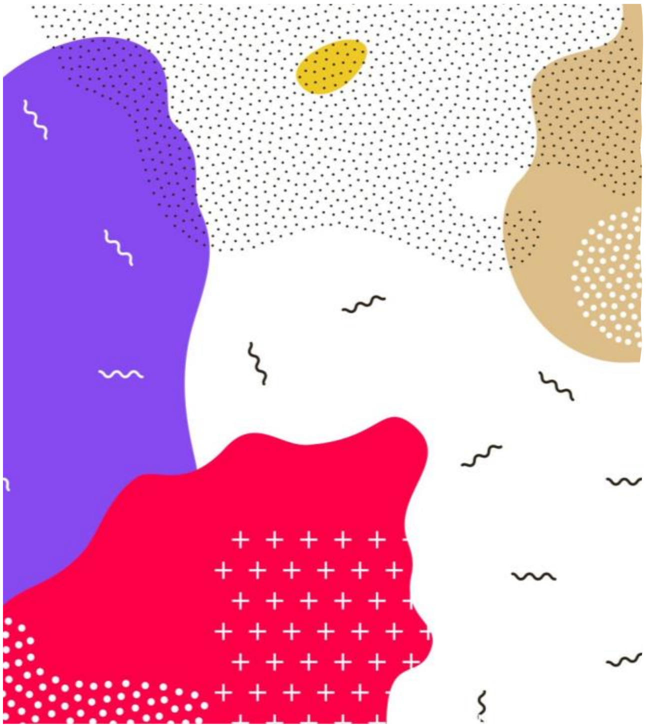

Green Chemistry and its Role for Sustainability

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GREEN CHEMISTRY

Green Chemistry is the **utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances** in the design, manufacture and application of chemical products .

Green Chemistry is a recent approach to design of energy efficient processes and the best form of waste disposal.

The awareness among the **organic chemists to practice green chemical routes for organic transformations is significantly increasing** in the place of mineral acids, mild solid acids or clays are used. The reactions are carried out in organized media or in green solvents.

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GREEN CHEMISTRY IS ABOUT

- Waste Minimization at Source
- Use of Catalysts in place of Reagents
- Using Non-Toxic Reagents
- Use of Renewable Resources
- Improved Atom Efficiency
- Use of Solvent Free or Recyclable Environmentally Benign Solvent systems

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Green Chemistry

- Green chemistry is the use of chemistry for pollution prevention
- Design of chemical products and processes that are more environmentally benign
- Reduction or elimination of the use or generation of hazardous substances associated with a particular synthesis or process
- **Green chemistry** looks at pollution prevention on the molecular scale and is an extremely important area of Chemistry due to the importance of Chemistry in our world today and the implications it can show on our environment
- The **Green Chemistry** program supports the invention of more environmentally friendly chemical processes which reduce or even eliminate the generation of hazardous substances

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Importance of Green Chemistry

- With the increase in production and use of chemical compounds, man has become more exposed to the deleterious effects. It is clear that the knowledge of toxicology is essential for the management and prevention of the adverse effects and toxicity of chemicals.
- 2 billion lbs. of chemicals were released into air, land and water (USEPA) in 1994
- Data includes only 365 of 70,000 chemicals available in commerce
- Environmental and hazardous wastes operations => economic burden
  - environmental expenditures : cost of doing business
  - **100-150 billion$ / year for remediation in US alone**
  - shift financial resources from costs to research & development
- Promise of Green Chemistry to lower overall costs associated with environmental health and safety

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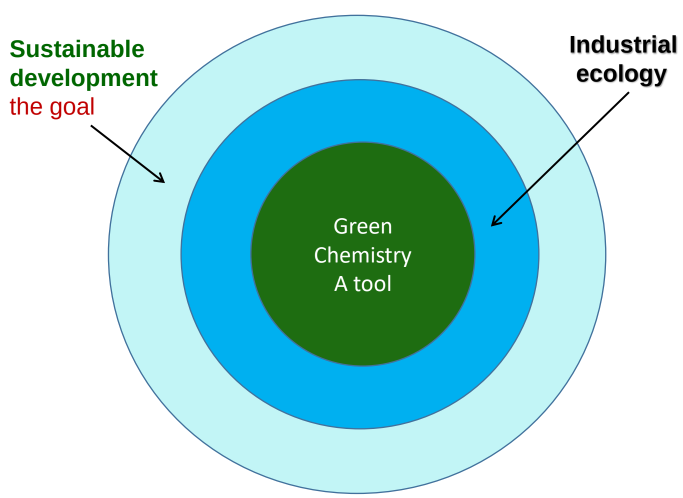
Green chemistry a tool

As human beings --- we are part of the environment

The way in which we interact with our environment influences the quality of our lives



Green chemistry, lies at the heart of the industrial ecology

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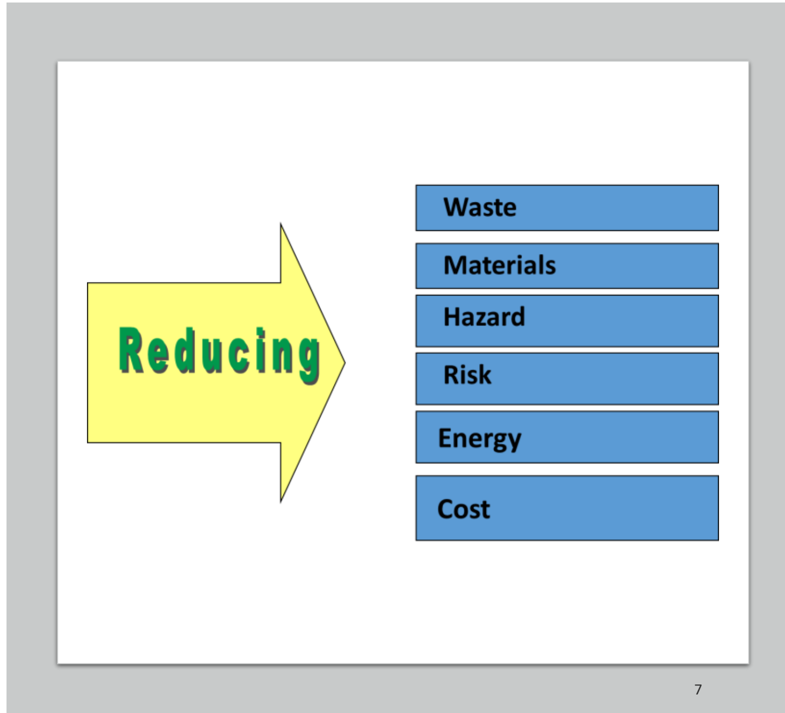
Green chemistry OR Benign chemistry OR Clean chemistry for sustainability

1- Synthesis (the path to making chemicals)

2- Processing (the actual making of chemicals)

3- Use of chemicals that reduce risks to humans and impact on the environment



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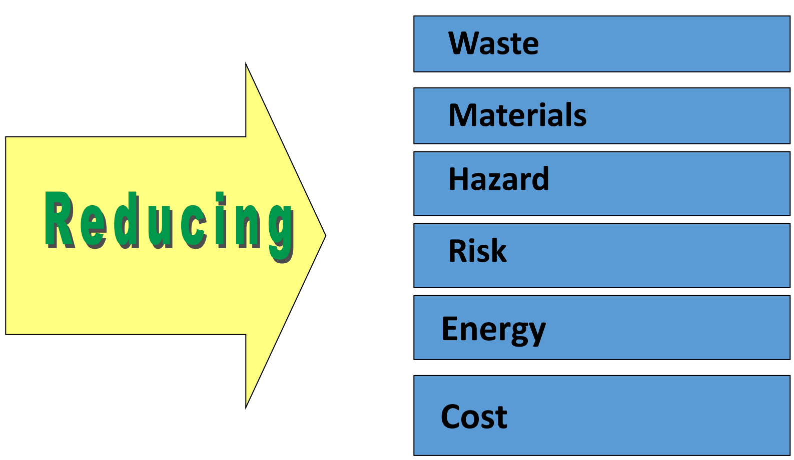
Green Chemistry Is About...



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Why do we need Green Chemistry ?

- Chemistry is undeniably a very prominent part of our daily lives.
- Chemical developments also bring new environmental problems and harmful unexpected side effects, which result in the need for 'greener' chemical products.
- A famous example is the pesticide DDT.
- Hundreds of tons of hazardous waste are released to the air, water and land by industry every hour of every day. The chemical industry is the biggest source of such waste.
- In recent years, pollution control board regulated to reduce harmful emissions , effluents and workers safety.

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The 12 Principles of Green Chemistry (1-4)

1. **Prevention**
   - It is better to prevent waste than to treat or clean up waste after it has been created.
2. **Atom Economy**
   - Synthetic methods should be designed to maximise the incorporation of all materials used in the process into the final product.
3. **Less Hazardous Chemical Synthesis**
   - Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to people or the environment.
4. **Designing Safer Chemicals**
   - Chemical products should be designed to effect their desired function while minimising their toxicity.

10

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The 12 Principles of Green Chemistry (5-8)

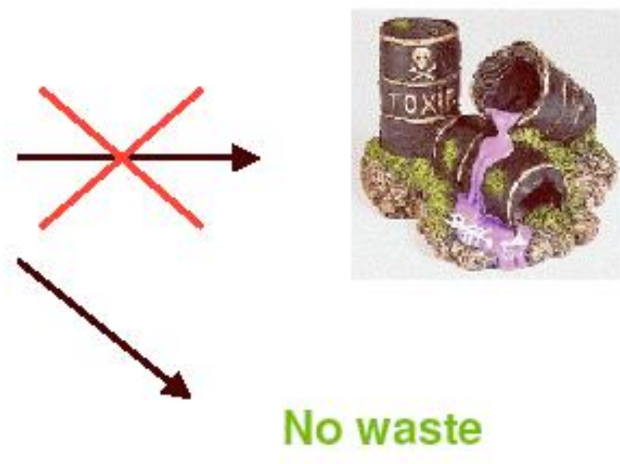
5. **Safer Solvents and Auxiliaries**
   - The use of auxiliary substances (e.g., solvents or separation agents) should be made unnecessary whenever possible and innocuous when used.
6. **Design for Energy Efficiency**
   - Energy requirements of chemical processes should be recognised for their environmental and economic impacts and should be minimised. If possible, synthetic methods should be conducted at ambient temperature and pressure.
7. **Use of Renewable Feedstocks**
   - A raw material or feedstock should be renewable rather than depleting whenever technically and economically practicable.
8. **Reduce Derivatives**
   - Unnecessary derivatization (use of blocking groups, protection/de-protection, and temporary modification of physical/chemical processes) should be minimised or avoided if possible, because such steps require additional reagents and can generate waste.

The 12 Principles of Green Chemistry (9-12)

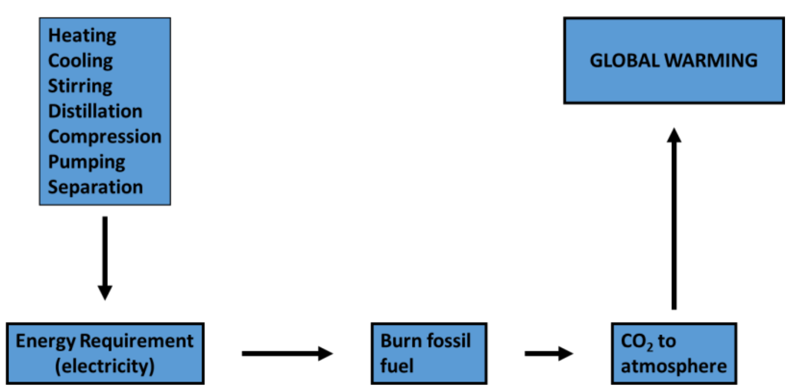
9. **Catalysis**
   - Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
10. **Design for Degradation**
    - Chemical products should be designed so that at the end of their function they break down into innocuous degradation products and do not persist in the environment.
11. **Real-time Analysis for Pollution Prevention**
    - Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.
12. **Inherently Safer Chemistry for Accident Prevention**
    - Substances and the form of a substance used in a chemical process should be chosen to minimise the potential for chemical accidents, including releases, explosions, and fires.

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

- **Chemical**
- **Process**



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



"A raw material of feedstock should be renewable rather than depleting wherever technically and economically practical"


Non-renewable


Renewable

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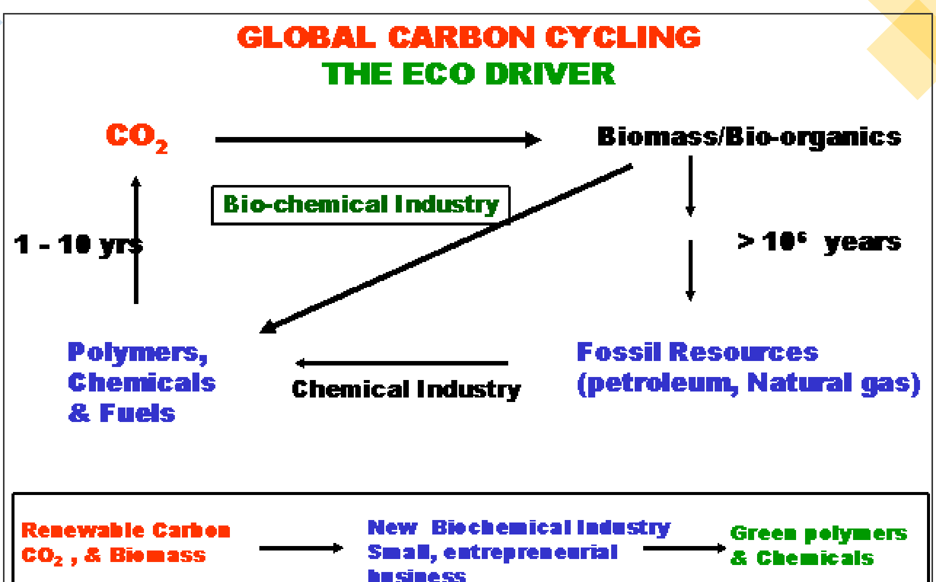


16

16

Resource Depletion

- Renewable resources can be made increasingly viable technologically and economically through green chemistry.

Biomass

Carbondioxide

Nanoscience

Solar

Waste utilization

17

Examples of green chemistry

- If the chemical reaction of the type

  $$A + B \longrightarrow P + W$$

- Find alternate A or B to avoid W

Disinfection of water:

- Disinfection of water by chlorination. Chlorine oxidizes the pathogens there by killing them, but at the same time forms harmful chlorinated compounds.
- A remedy is to use another oxidant, such as

18

Production of allyl alcohol

- **Traditional route:** Alkaline hydrolysis of allyl chloride, which generates the product and hydrochloric acid as a by-product

$$CH_2{=}CHCH_2Cl + H_2O \longrightarrow CH_2{=}CHCH_2OH + HCl$$

problem product

- **Greener route, to avoid chlorine:** Two-step using propylene ($CH_2{=}CHCH_3$), acetic acid (CH_3COOH) and oxygen (O_2)

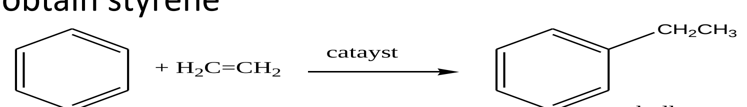
$$CH_2{=}CHCH_3 + CH_3COOH + 1/_2\ O_2 \longrightarrow CH_2{=}CHCH_2OCOCH_3 + H_2O$$

$$CH_2{=}CHCH_2OCOCH_3 + H_2O \longrightarrow CH_2{=}CHCH_2OH + CH_3COOH$$

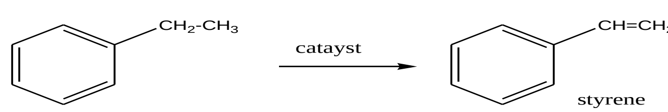
- **Added benefit:** The acetic acid produced in the 2nd reaction can be recovered and used again for the 1st reaction, leaving no unwanted by-product.

Production of styrene

- **Traditional route:** Two-step method starting with benzene, (which is carcinogenic) and ethylene to form ethylbenzene, followed by dehydrogenation to obtain styrene

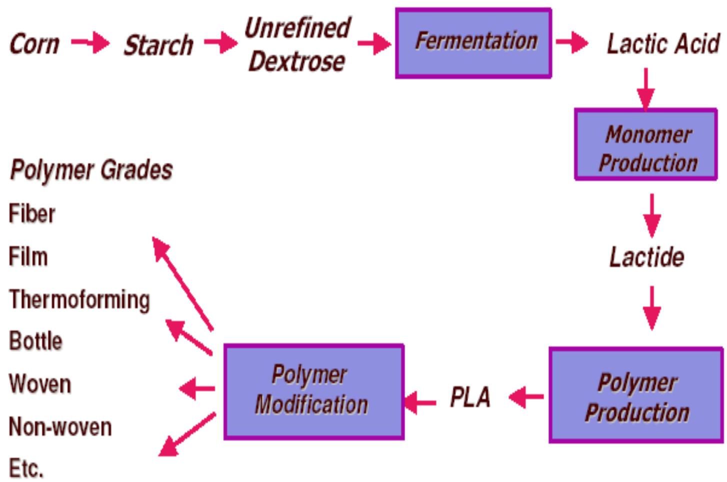


- **Greener route:** To avoid benzene, start with xylene (cheapest source of aromatics and environmentally safer than benzene).



- Another option, still under development, is to start with toluene (benzene ring with CH_3 tail).

Poly lactic acid (PLA) for plastics production



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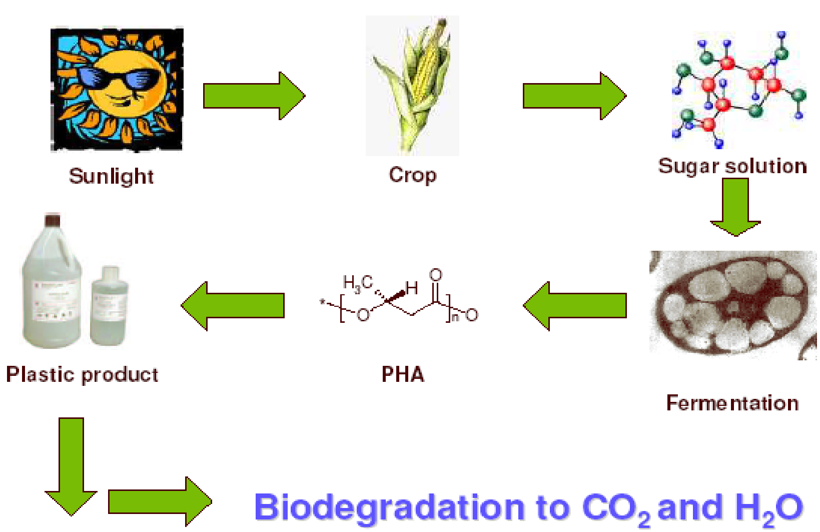
21

Polyhydroxyalkanoates (PHA's)



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22

Ibuprofen

Ibuprofen is a common analgesic and anti-inflammatory drug used widely.

About 30 million lb of ibuprofen are synthesized annually by Boots method. It will produce more than 35 million lb of waste product.

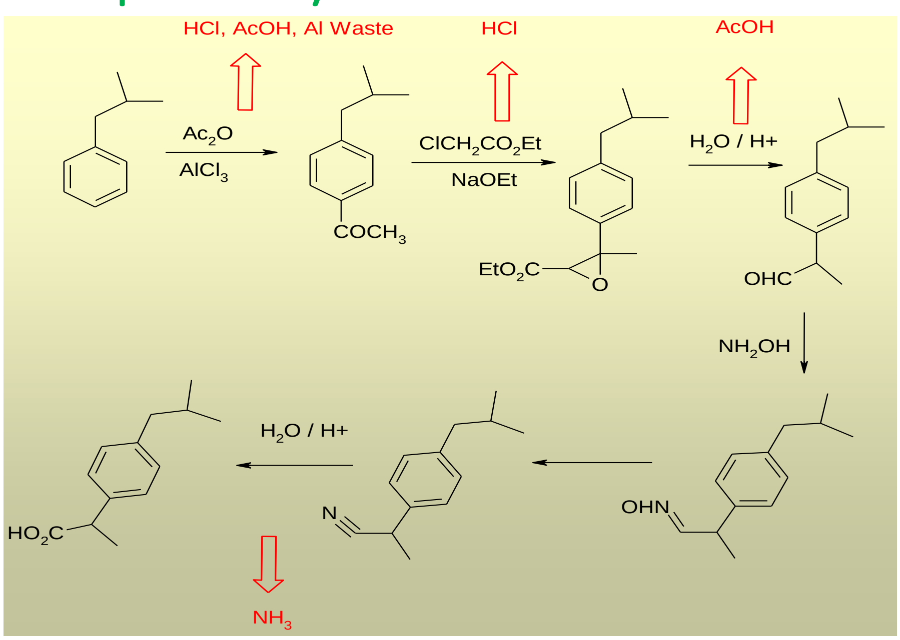
The greener synthesize by BHC (Boots and Hoechst-Celanese Company) can dramatically reduce this waste product generation.

“To Know, is to know that you know nothing. That is the meaning of true knowledge” - Socrates

23

23

Ibuprofen Synthesis Classic Route



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24

Ibuprofen Synthesis Classic Route

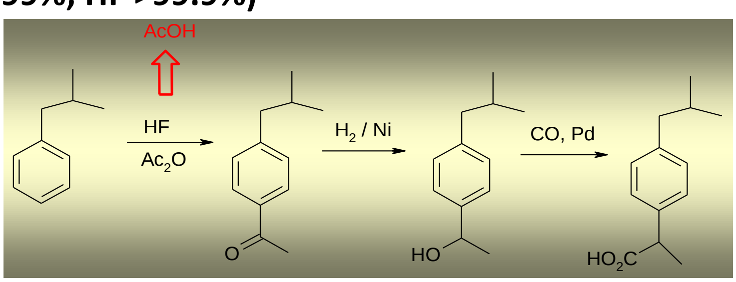
- Atomic Economy: **32%**
- If this synthesis were to be used today, the amount of by-products per year:

27,000 TPY

MORE WASTE THAN PRODUCT!!!

Boots & Hoechst Synthesis of Ibuprofen – Green Route

Developed to improve production:
* 3 steps
* No solvents
* Catalytic vs. stoichiometric reagents
* Recycling, reuse and recovery of byproducts and reagents (**acetic acid>99%; HF >99.9%)**



Boots & Hoechst Synthesis of Ibuprofen – Green Route

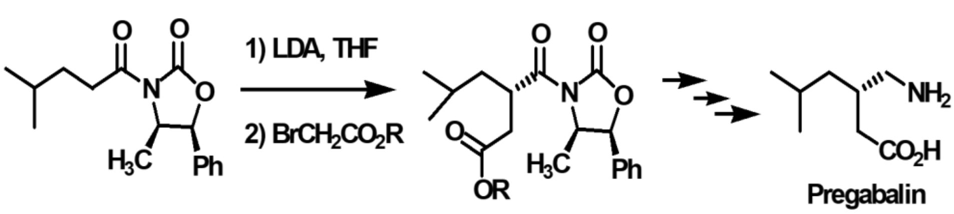
- Atomic Economy 77%
- Faster
- More % yield
- Less waste produced

- "Wisdom begins in wonder" - Socrates

27

27

Medicinal Chemistry Pregabalin Synthesis

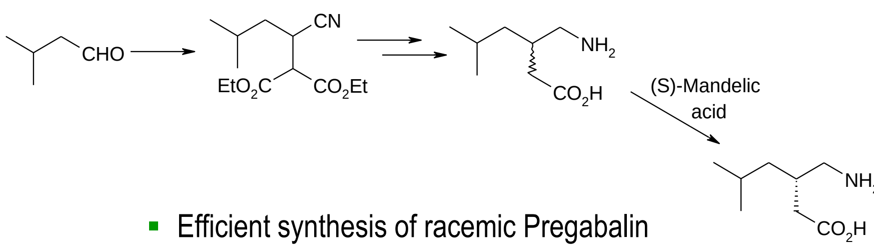


- 10 steps, 33% overall yield
- Cost was 6x target
- Silverman et al. Synthesis, 1989, 953. (racemic synthesis)
- Yuan et al., Biorg. Med. Chem. Lett., 1991, 34, 2295 (chiral synthesis shown on slide).

28

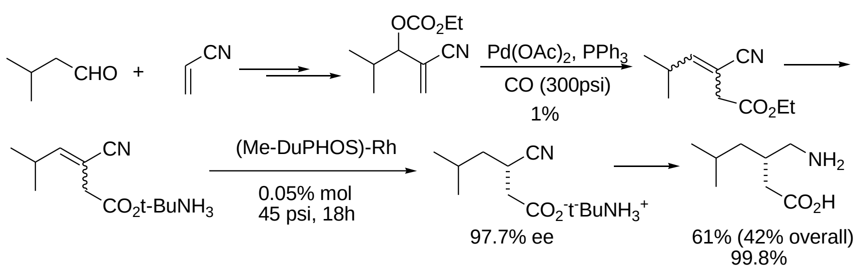
28

Pregabalin (Lyrica®) Launch Process

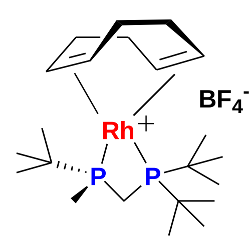


- Efficient synthesis of racemic Pregabalin
- Final Step Classical Resolution
- Wrong enantiomer difficult to recycle
- E-Factor 86
- Chemistry Published (Org. Process R and D, 1997, 1, 26)

Asymmetric Hydrogenation Route

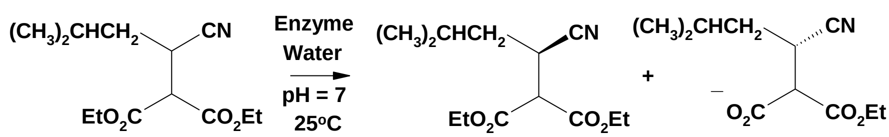


- Higher yield (42% overall)
- Original Catalyst (Me-DuPHOS-Rh, S/C ratio 2700)
- Licensed chiral ligand expensive
- Much improved environmental profile but similar cost to resolution route.
- Chemistry Published (2004JACS5966) (2003JOC5731)



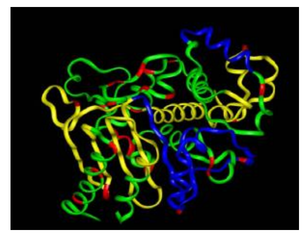
(S)-[Rh-Trichickenfootphos]

Enzymatic Resolution of CNDE



Racemic Diester — R-Diester Organic Soluble — S-Monoester Water Soluble

- **Enzymatic hydrolysis of Cyano diester enabled early resolution of chiral center**
- **Enzyme screen revealed 2 (*S*)-selective hits with E>200:**
  - ***Thermomyces lanuginosus* lipase (Novozymes)**

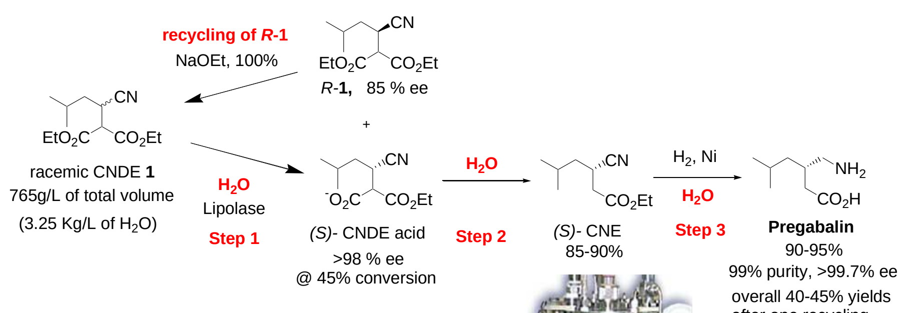


  - Rhizopus delemar lipase (Amano)

31

31

Biocatalytic Kinetic Resolution Route



- Biocatalytic with low (~0.8%) protein loading
- Resolution at first step (wrong enantiomer can be recycled)
- High throughput; simple operations
- All 4 reactions conducted in water
- Enzymatic Step scaled up to 10, 000 Kg scale
- E-Factor improved from 86 to 17

32

32

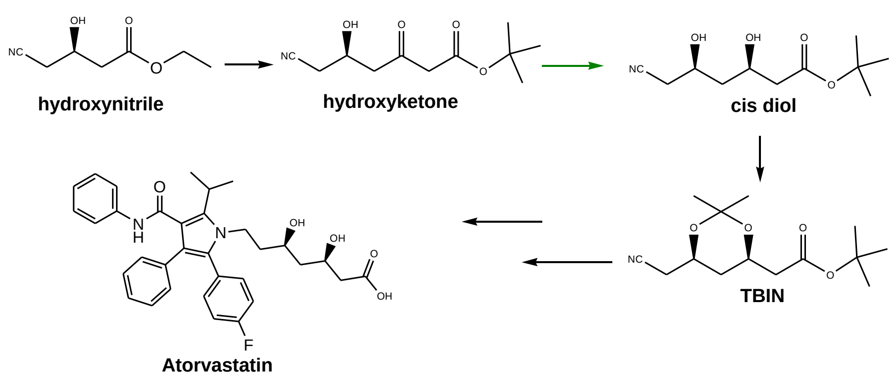
Atorvastatin

- Atorvastatin, marketed under the trade name Lipitor among others, is a member of the drug class known as statins, which are used primarily as a lipid-lowering agent and for prevention of events associated with cardiovascular disease.
- Like all statins, atorvastatin works by inhibiting HMG-CoA reductase, an enzyme found in liver tissue that plays a key role in production of cholesterol in the body.

33

33

New Process for Atorvastatin (Lipitor®)

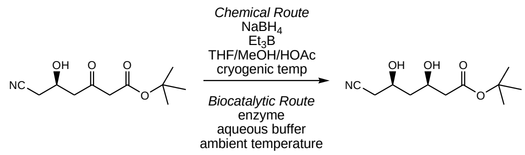


- The reduction of hydroxyketone to cis diol is a key step that sets the stereochemistry for atorvastatin. This step has now been converted from a chemical reduction to a biocatalytic reduction

34

34

Comparison of Chemical and Biocatalytic Reactions



- Chemical process is slow: 80 hours for 6 x methanol distillations to remove the boron based waste. Enzymatic reaction takes <24 hours with a relatively simple work-up.
- Quality: Enzymes are highly selective, giving improved cis: trans ratio.
- Triethyl Borane: pyrophoric and toxic
- $NaBH_4$: Safety hazard. H_2 source.
- Multiple solvents and low temperature requirement eliminated

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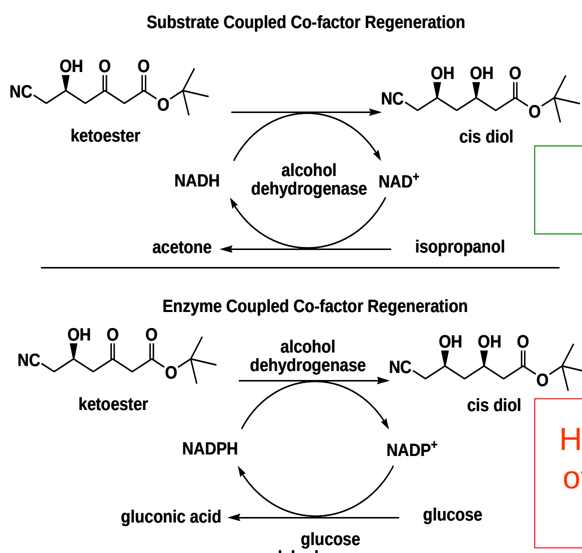
Co-factor Recycling Systems



Greener Option

High Levels of Aqueous Waste

36

36

The major uses of GREEN CHEMISTRY

- Energy
- Global Change
- Resource Depletion
- Food Supply
- Toxics in the Environment

37