CHEM 489 – Spring 2020
Advanced Environmental Chemistry
Introduction to Green Chemistry
Dr. Brush

February 4 (Tuesday):

- **Writing Prompt-2 due <u>yesterday</u>**
- **Worksheet-1 due <u>today</u>**
- **Journal Club-2 info due <u>today</u>**
- **Journal Club-2 presentations <u>Thursday</u>**
- **Introduction to Green Chemistry (continued):**
    - ➢ **Green Chemistry Metrics**

GREEN
CHEMISTRY

Green Chemistry Metrics for Reaction Efficiency – Molecular Design

"Green chemistry is an approach to chemistry that aims to **maximize efficiency** and **minimize hazardous effects** on human health and the environment. While no reaction can be perfectly "green", the overall negative impact of chemistry research and the chemical industry can be reduced by implementing the 12 Principles of Green Chemistry wherever possible." Compound Interest, WWW.COMPOUNDCHEM.COM

Risk = Hazard x Exposure x Vulnerability

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Green Chemistry Metrics for Reaction Efficiency – Molecular Design

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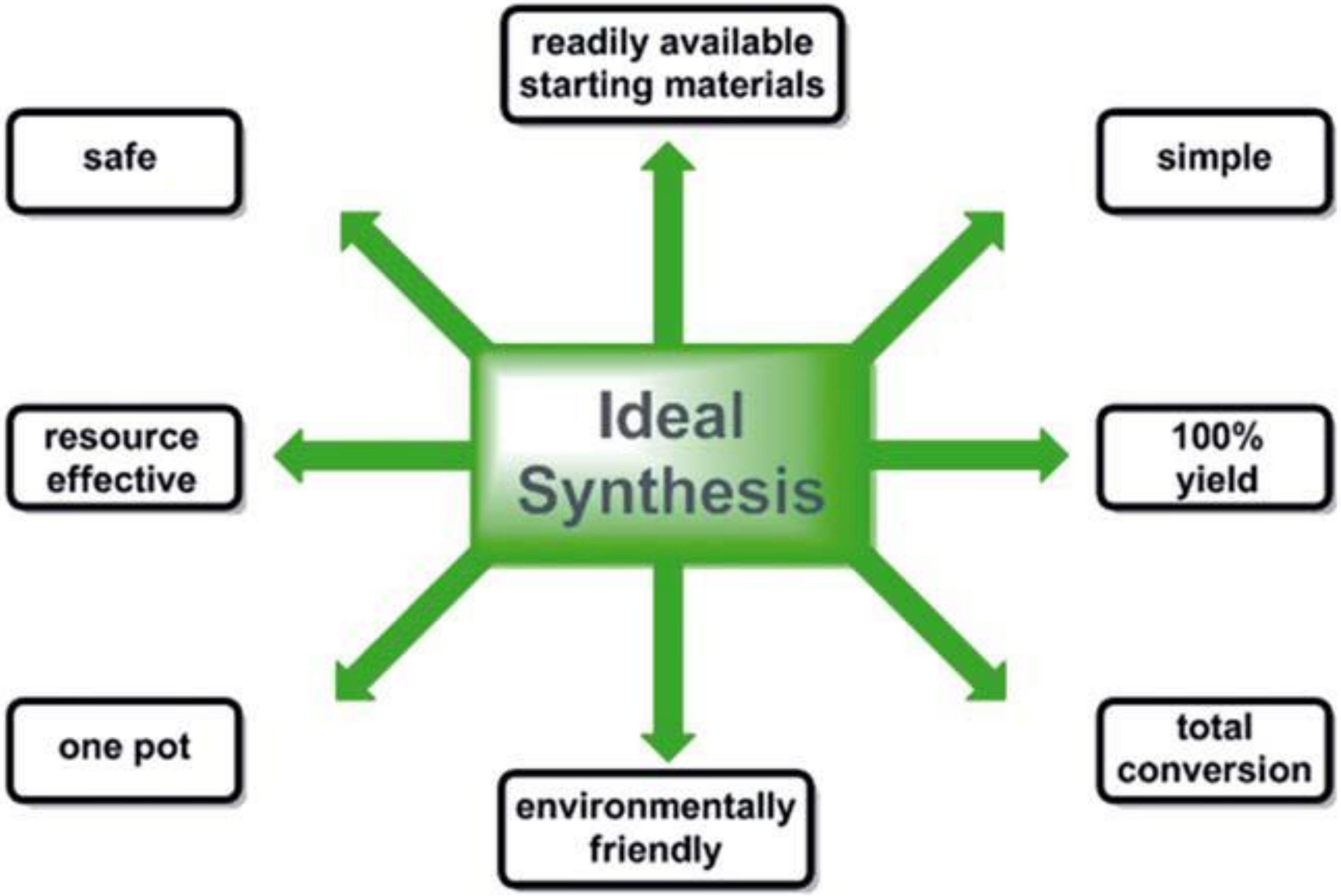
12 Principles of Green Chemistry

1) Prevention
2) Atom Economy
3) Safe Processes
4) Safer Chemicals
5) Safer Solvents
6) Energy Efficiency
7) Renewable Feedstocks
8) Reduce Derivatives
9) Catalysis
10) Bio-degradation
11) Real-time analysis
12) Accident Prevention

Green Chemistry Metrics for Reaction Efficiency

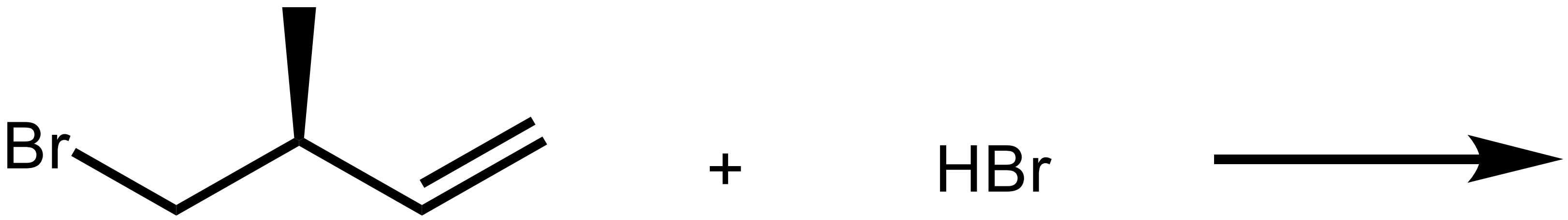
Metrics based on:

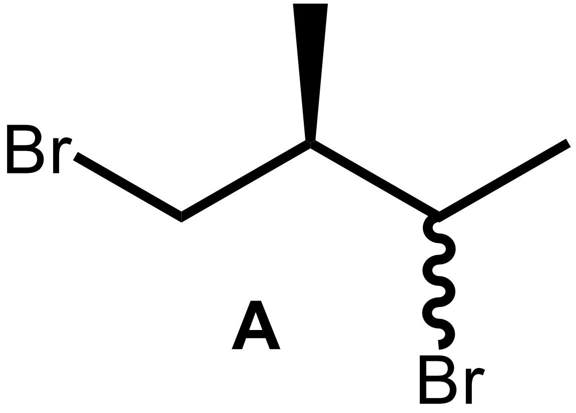
- Chemical yield
- Maximizing resource efficiency (Atom Economy)
- Minimizing waste
- Avoiding the use of hazardous and toxic chemicals.



Efficiency Metrics for Chemical Processes

(1) Selectivity: Controlling reactions to give the desired product over competing products or stereoisomers: Chemoselectivity, Regioselectivity, Stereoselectivity.





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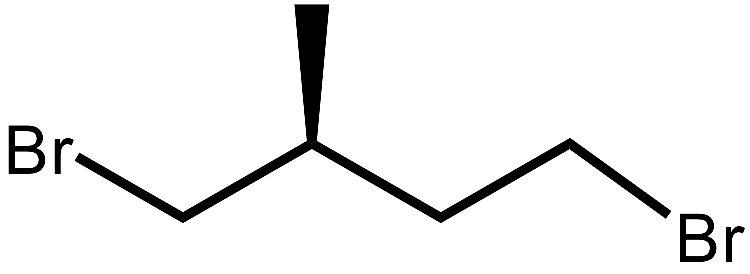

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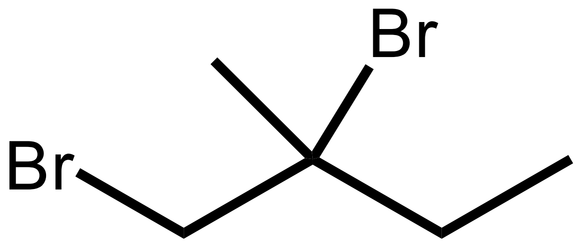

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Efficiency Metrics for Chemical Processes

(2) % Yield: Comparing the amount of product formed to the limiting reagent (based on the theoretical yield of product).

$$\% \text{ Yield} = \frac{\text{Experimental yield of product}}{\text{Theoretical yield}} \times 100$$

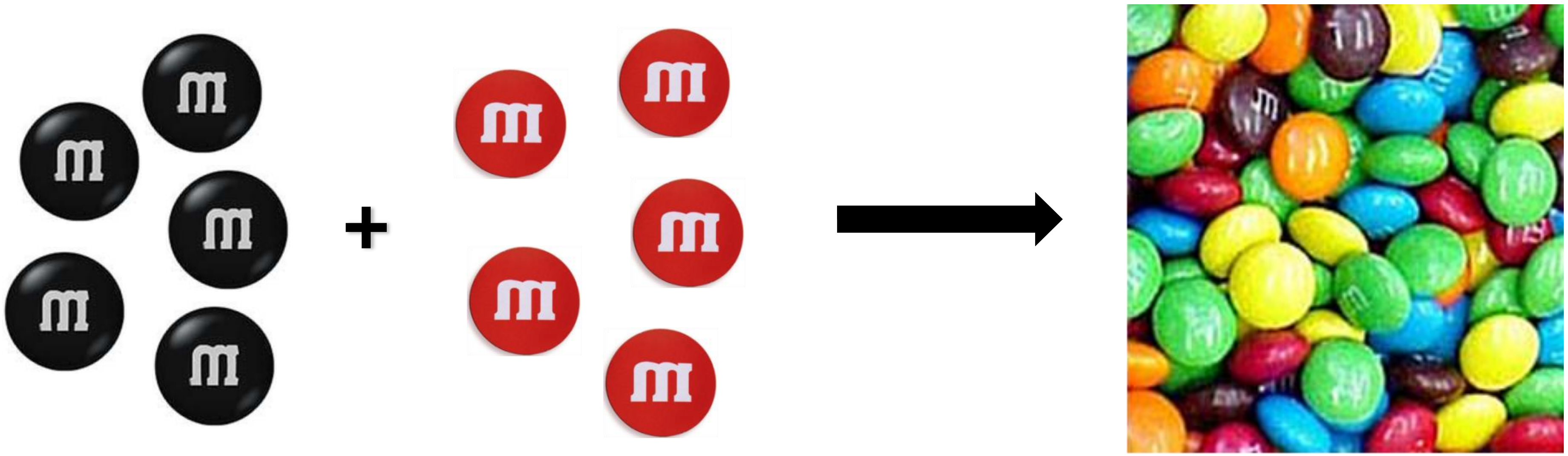
Efficiency Metrics for Chemical Processes

(3) Atom Economy: Designing a synthesis in which most, or all, of the atoms of reactants become incorporated into the final product.

$$\% \text{ Atom Economy} = \frac{\text{Formula weight of product}}{\Sigma\,(\text{Formula weight of all reactants})} \times 100$$

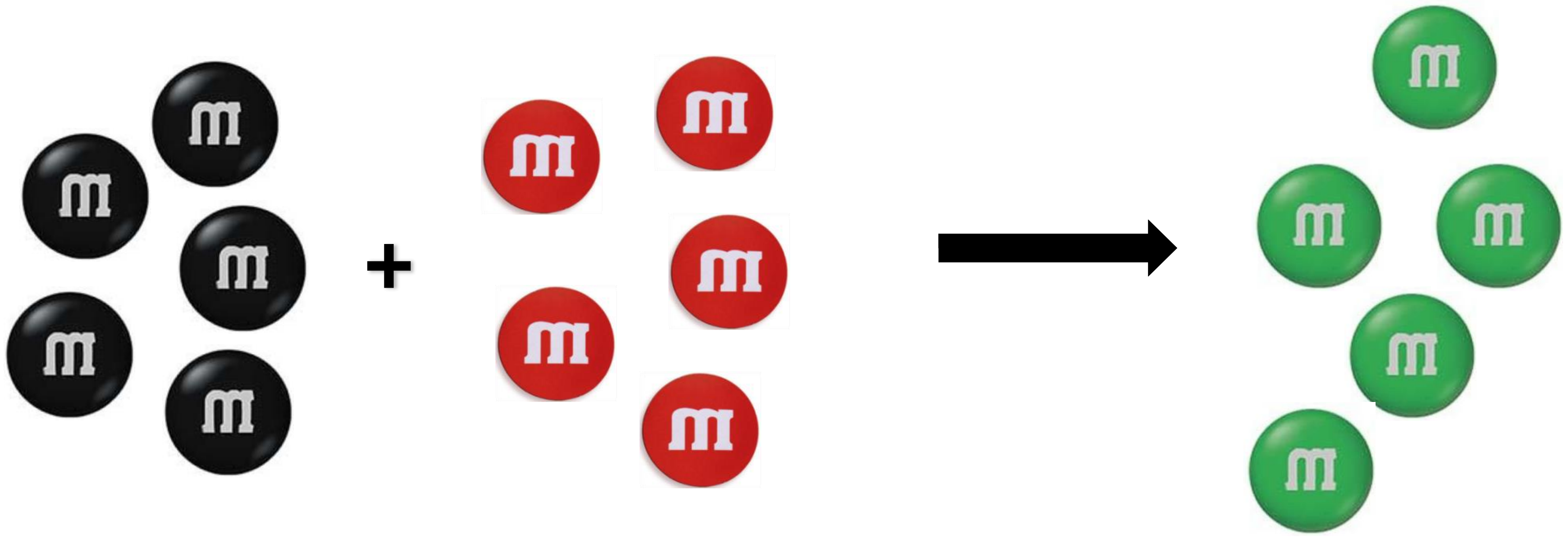
*****You can have a very high % Yield, but a low Atom Economy.**

In the real world……



atom economy = ___30___%

An Efficient "Green" Reaction



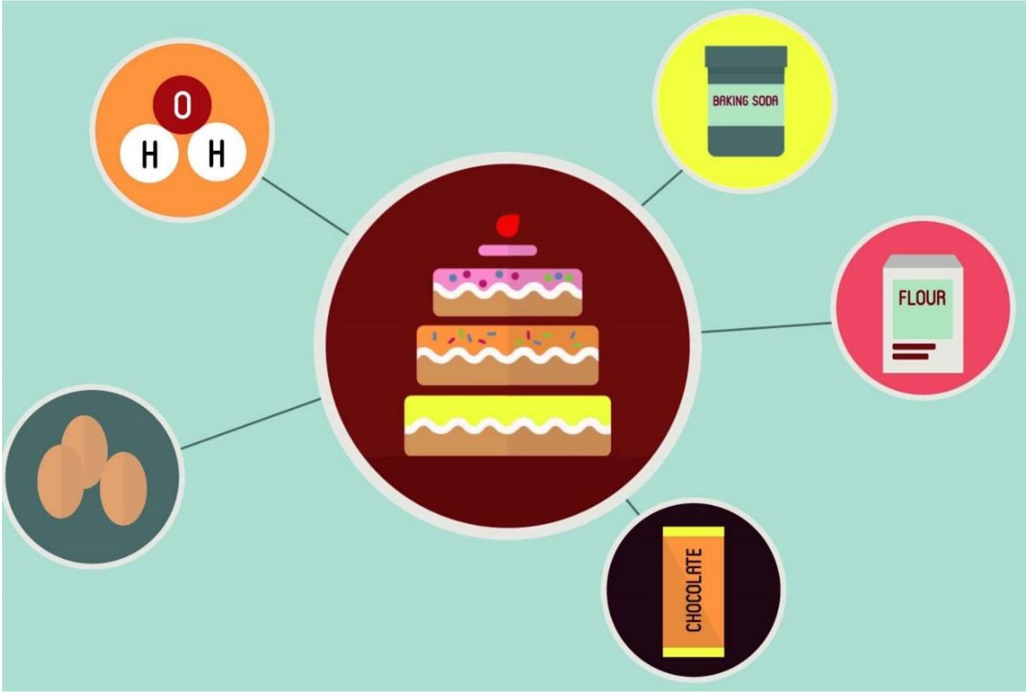
Atom Economy = 100%

Waste = 0

Atom Economy – Advantages & Disadvantages

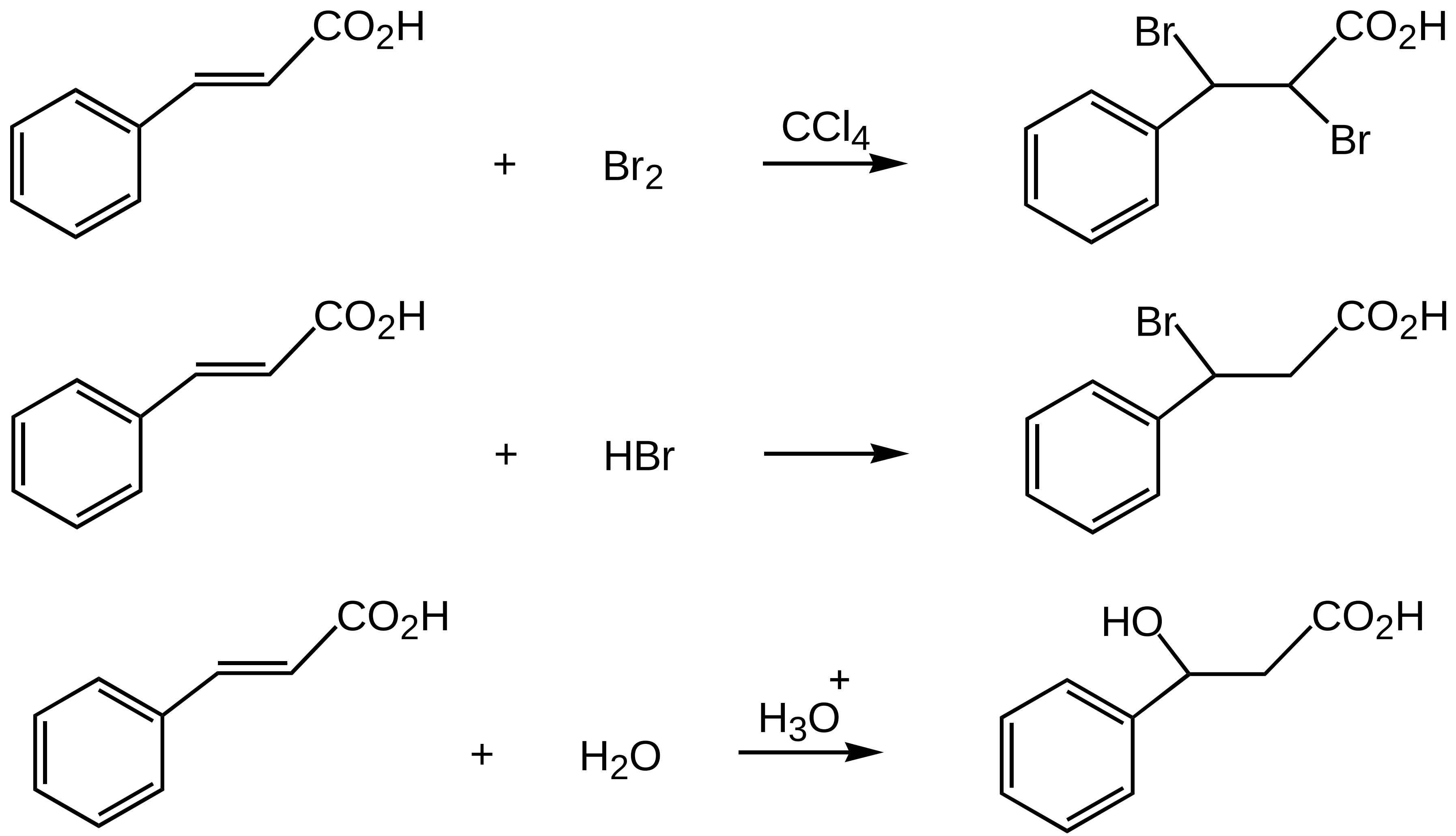
- Atom Economy is a theoretical number which assumes: (1) exact stoichiometric quantities of starting materials; (2) a chemical yield of 100%; and (3) disregards substances, such as solvents and chemicals used in the work-up of the reaction mixture, which do not appear in the stoichiometric equation.

- Useful tool for rapid evaluation, before any experiments are performed.
- Prediction of resource efficiency – amount and types of waste that will be generated.



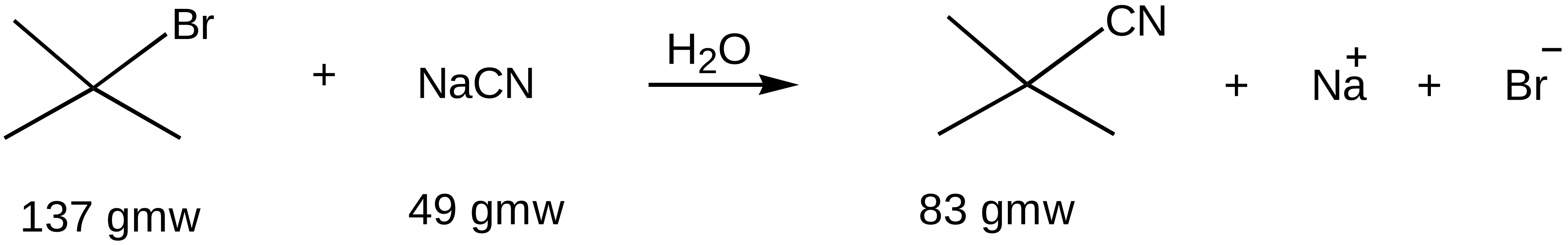
Atom Economy of Common Reactions

Electrophilic Addition. Atom Economy ca. 100%!



Atom Economy of Common Reactions

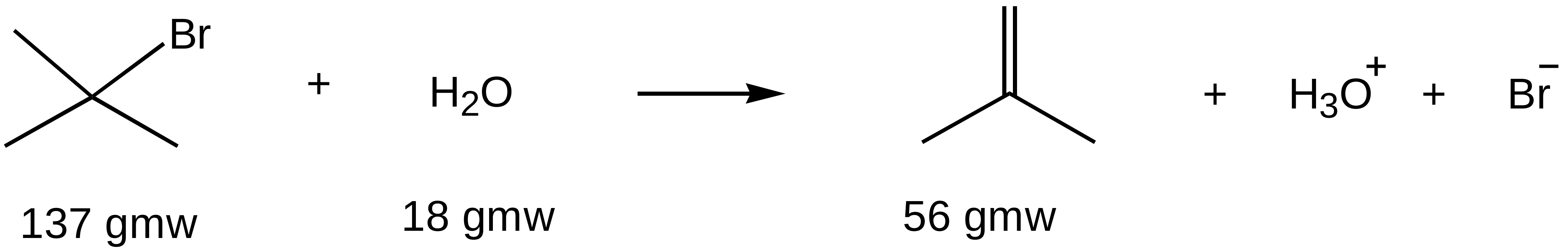
Substitution: SN1 vs SN2



Atom Economy = 44%

Atom Economy of Common Reactions

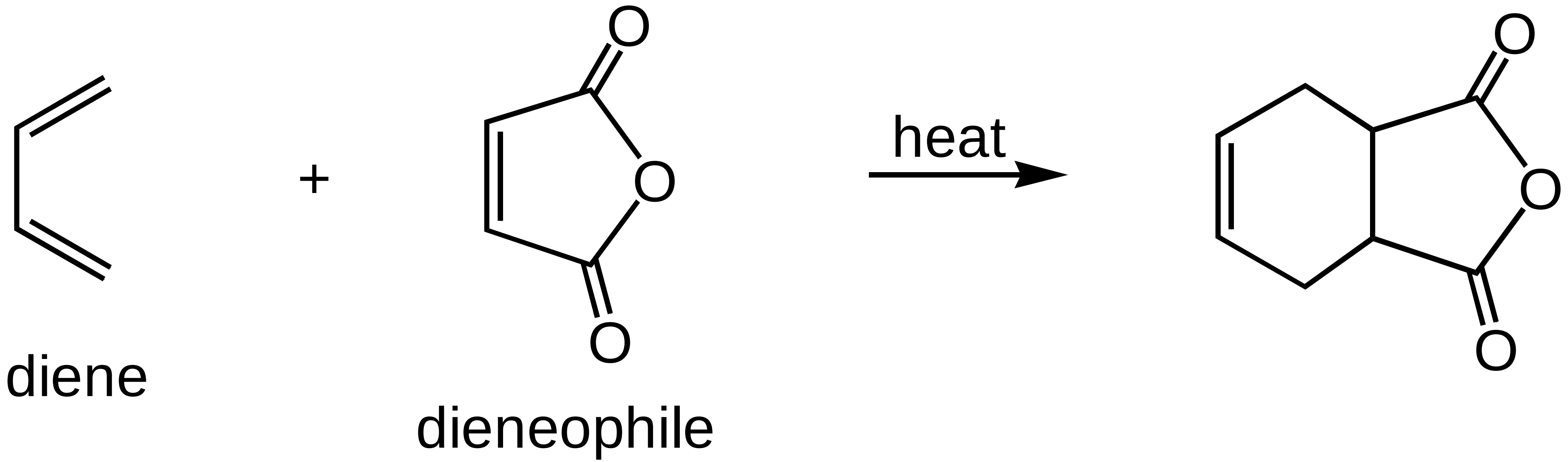
Elimination: E1 vs E2



Atom Economy = 36%

Atom Economy of Common Reactions

Diels-Alder Reaction: Atom Economy = 100%



Efficiency Metrics for Chemical Processes

(4) Process Mass Intensity (PMI): Compares total mass used in a process to mass of product.

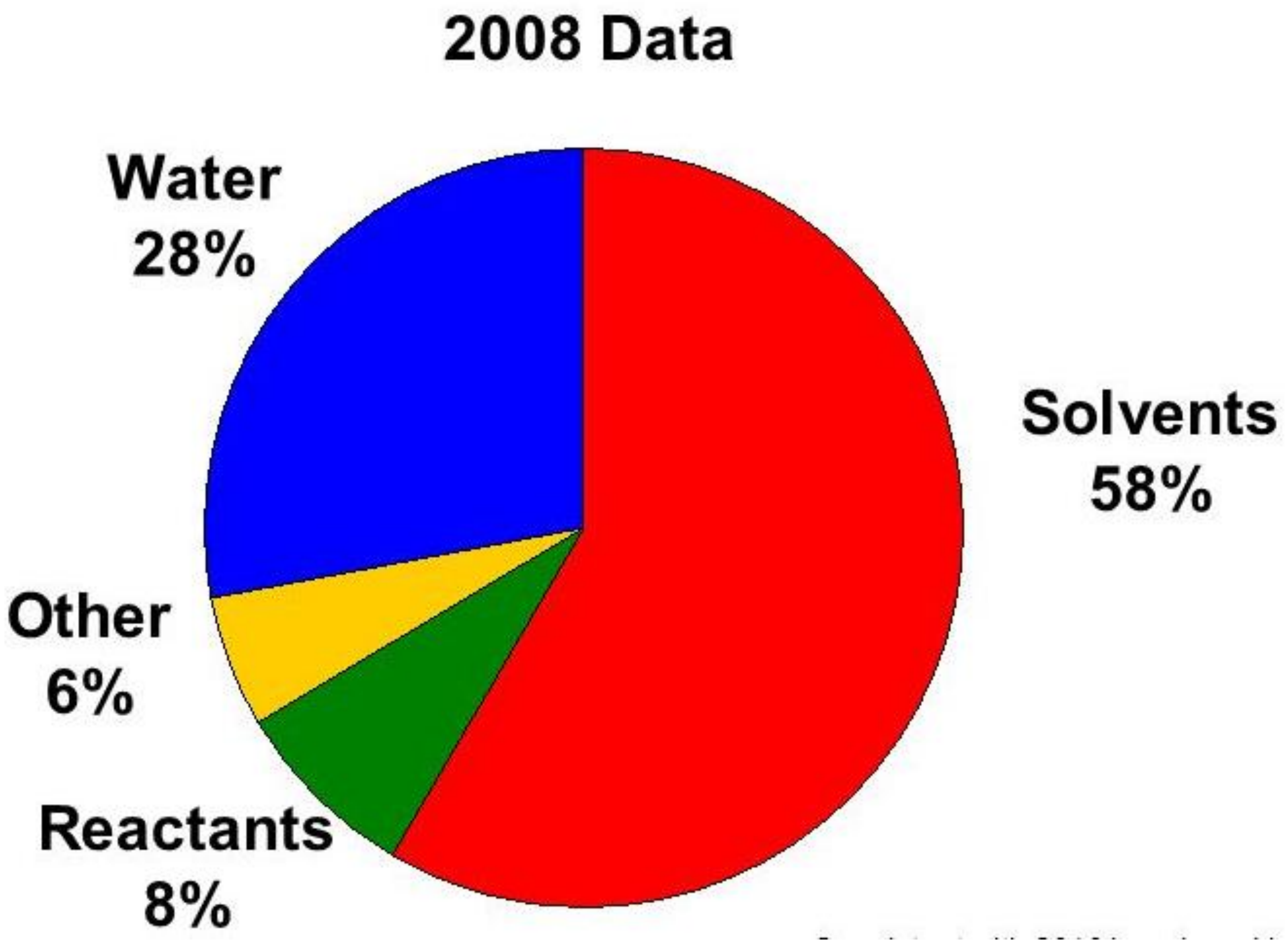
$$\text{PMI} = \frac{\text{Total mass used in a process (kg)}}{\text{Mass of final product (kg)}}$$

Process Mass Intensity (PMI)

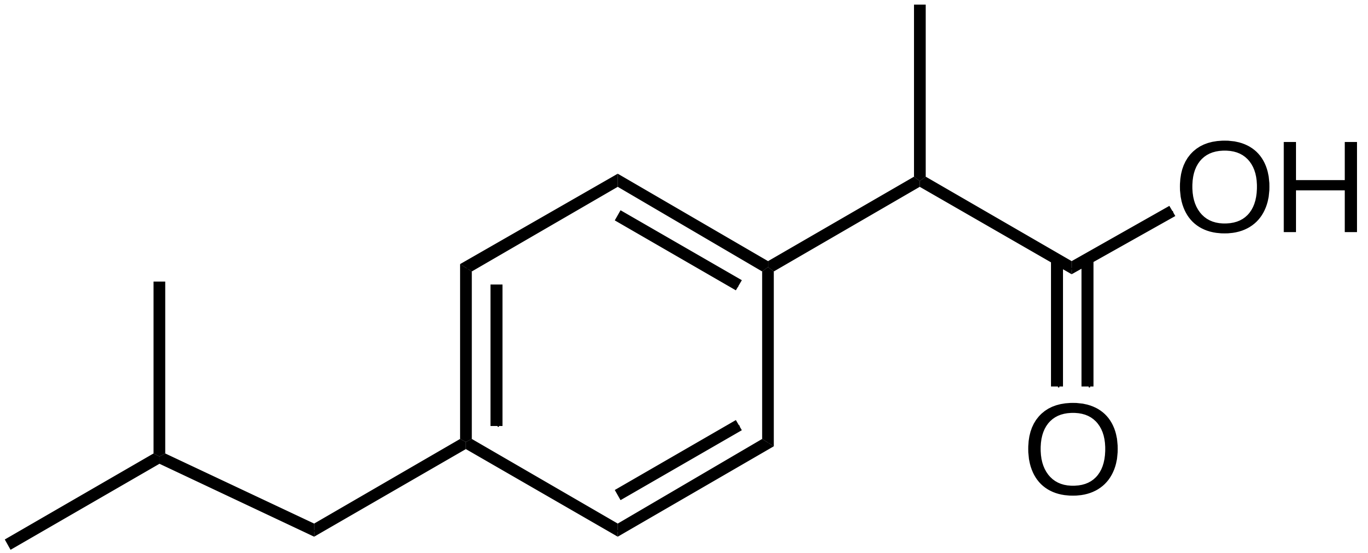
$$\text{PMI} = \frac{\text{Total mass used in a process (kg)}}{\text{Mass of final product (kg)}}$$

- **Mass used in the process includes reagents, solvents, catalysts, water, etc.**
- **Evaluate human and environmental impact of waste**
- **The ideal PMI is 1 (kg/kg).**
- **Tens of kgs waste per kg product typical of the fine chemicals industry**

Process Mass Intensity – Pharmaceutical industry



Class Exercise – Applying Assessment Metrics:
Synthesis, Production and Use of Ibuprofen



ibuprofen

Process Assessment

- Why is the product needed, who needs it, and why?
- Risk Assessment: Hazards x Exposure x Vulnerability inherent in the Product, Waste, and Reagents; harmful to people, environment?
- Use 12 Principles of Green Chemistry or other metric?
- Selectivity, % yield, % atom economy, PMI
- Renewable or non-renewable resources; water & electricity usage; source of resources?

Ibuprofen

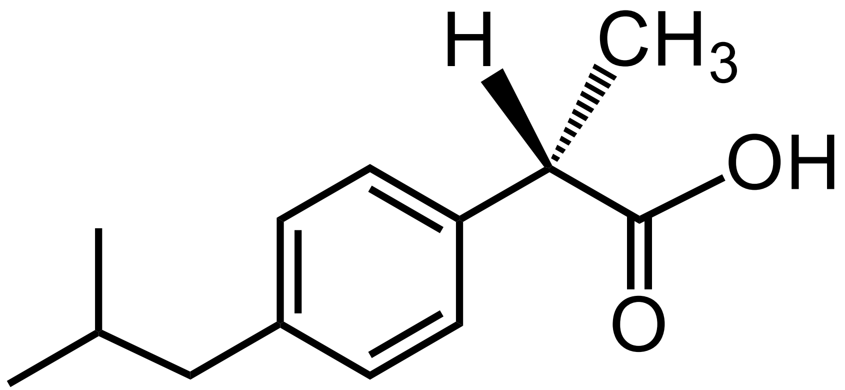
•Analgesic pain reliever that is the active ingredient in Advil, Motrin, Medipren & Nuprin.

•Also effective as a non-steroidal anti-inflammatory drug (NSAID). NSAID's reduce swelling and inflammation in arthritis, osteoarthritis and rheumatism.

•Over 30 million lbs produced worldwide per year.

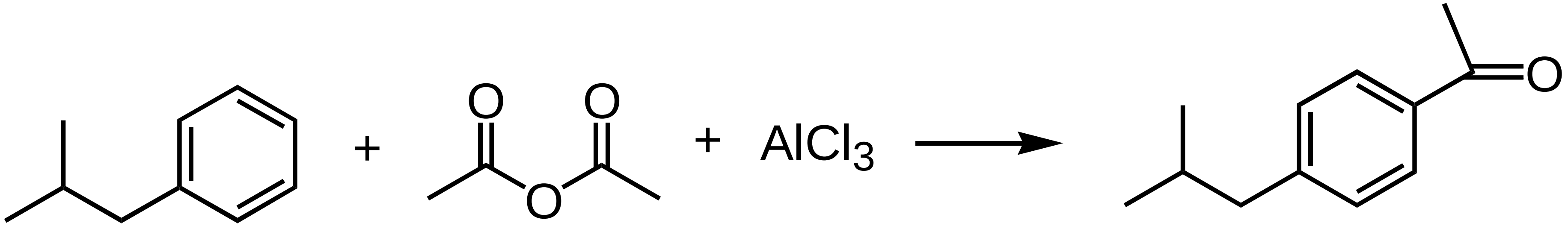
•Has been detected in wastewater; environmental impact unknown.

•Estimated that the conventional synthesis method produces over 40 million lbs of waste per year.

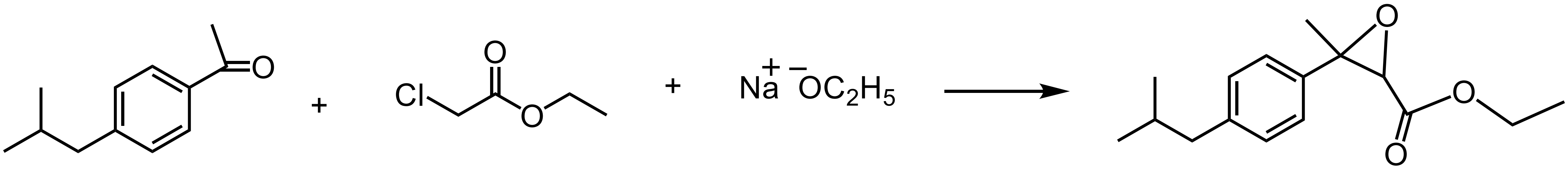


ibuprofen

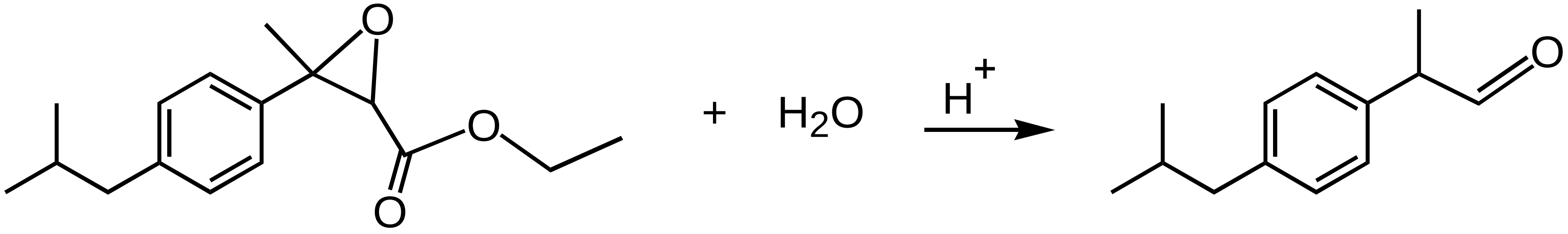
Traditional Ibuprofen Synthesis



(1) Friedel-Crafts acylation: AE = 48%

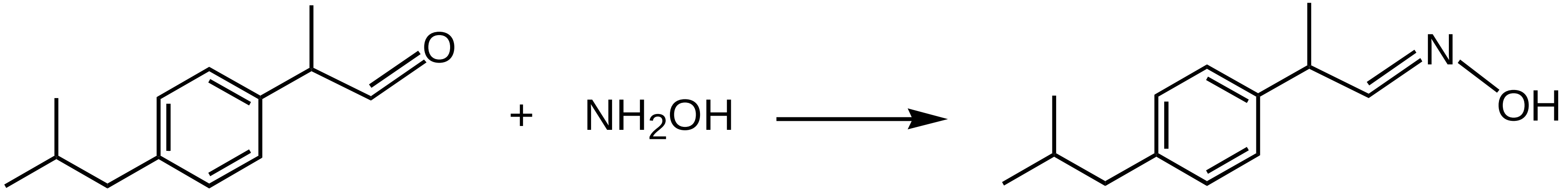


(2) Condensation: AE = 71%

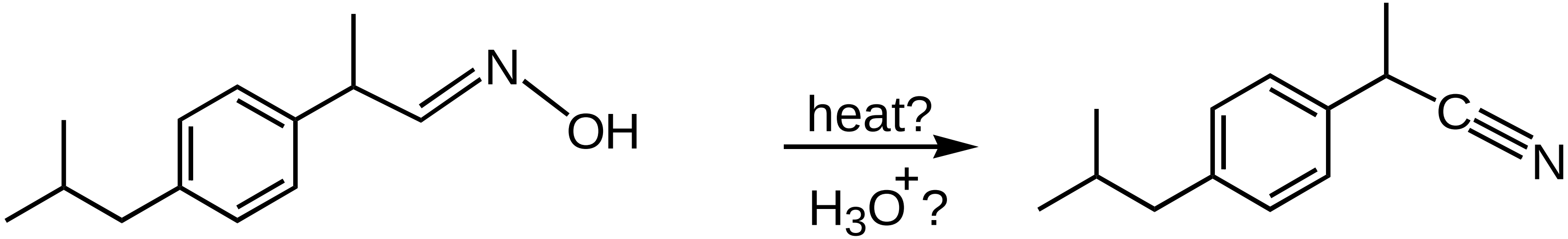


(3) Hydrolysis/Elimination: AE = 67%

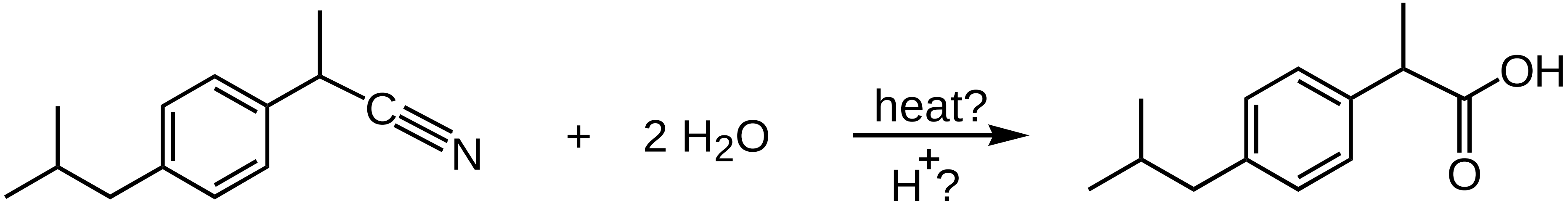
Traditional Ibuprofen Synthesis (cont.)



(4) Addition/Elimination: AE = 92%



(5) Dehydration: AE = 91%



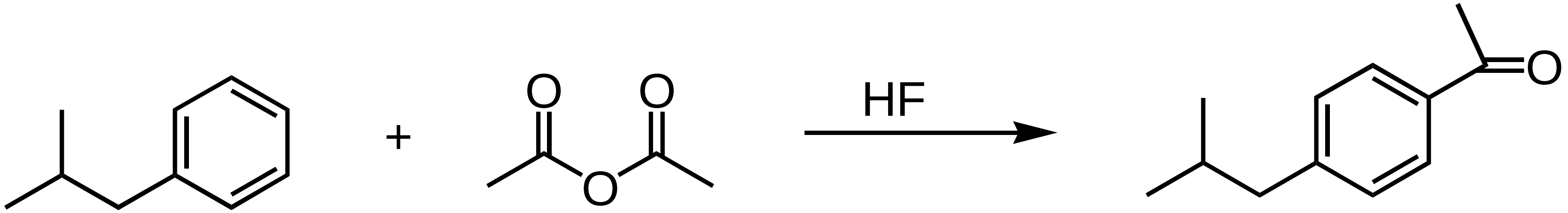
ibuprofen

(6) Hydrolysis: AE = 92%

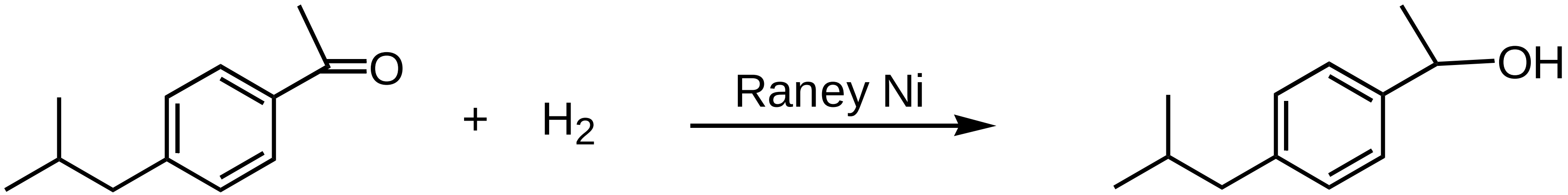
Traditional Ibuprofen Synthesis - Summary

- Each of the 6 steps has ca. 90% yield, but the overall yield is 40%
- Overall Atom Economy = 32% (68% waste!)
- Produces large quantities of secondary byproducts and unrecycled chemical waste (>40 million lbs).
- $AlCl_3$ in step (1) is not used as a catalyst but in stoichiometric amounts, producing large quantities of aluminum trichloride hydrate waste (landfill).
- Six step synthesis requires larger production plants, more capital, more energy & water, increased potential for problems with maintenance and higher risk.

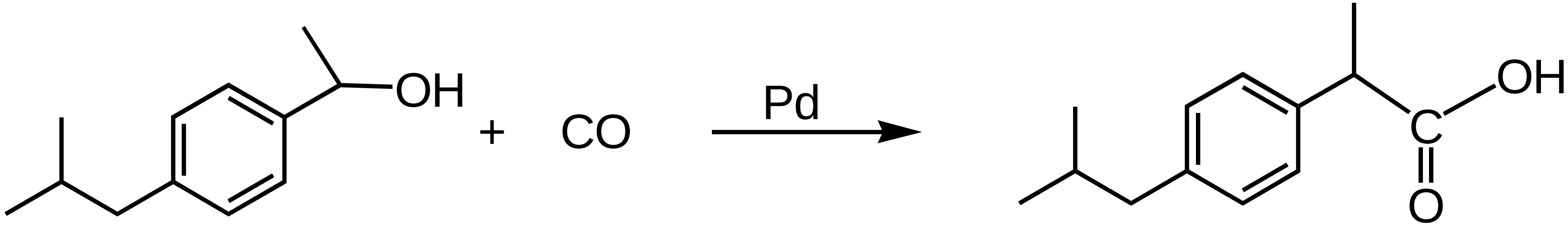
BHC Company Ibuprofen Synthesis (patented 1991)



(1) Friedel-Crafts acylation: AE = 75%.



(2) Catalytic Hydrogenation: AE = 100%.



(3) Carbonylation: AE =100%.

Ibuprofen!

BHC Ibuprofen Synthesis - Summary

- **Same starting compound in each synthesis (2-methyl-1-phenyl propane)**
- **Overall Atom Economy = 80%**
- **>99% of the HF and acetic acid byproduct in step (1) are recovered and recycled, so Atom Economy ~ 100%.**
- **All three steps are catalytic, and the catalysts (Raney Ni, Pd) are recovered and reused; less auxiliaries (lower water & energy usage).**
- **Three step synthesis means greater throughput, and ability to generate larger quantities of ibuprofen in less time with less capital expenditure. Cheaper!**
- **Overall yield is 77%**