Research In Green Organic Chemistry: The Design of Greener Undergraduate Labs

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CHE 498

Outline

- Green Chemistry
- Research Objectives
- Green Considerations
- My Research
  - Synthesis of Acetylsalicylic Acid
  - Esterification by Azeotropic Distillation
- Experimental Results
- Green Aspects

Green Chemistry

- The Utilization of a set of principles that reduces or eliminates the use and/or generation of hazardous substances in the design, manufacture, and application of chemical compounds.
- The Goal is to make reactions safer, more efficient, and more cost effective while minimizing personal and environmental harm.

My Research Objectives

- Develop greener organic chemistry labs that can be performed safely and effectively by undergraduate students.
- Labs must incorporate CHE 305/306 course material.
- Labs must meet the goals of Green Chemistry.

Green Considerations

- Replace hazardous reagents with safer renewable reagents
- Minimize or eliminate the generation of hazardous waste and products
- Avoid auxiliary substances, such as solvents, whenever possible.
- Use reagents catalytically rather than stoichiometrically

Green Consideration Continued…

- Minimize energy use
- Maximize the incorporation of all starting materials used into the final product (Atom Economy).
- Develop procedures that can be performed on an open bench top
- Generate products and by-products that can be recycled or reused

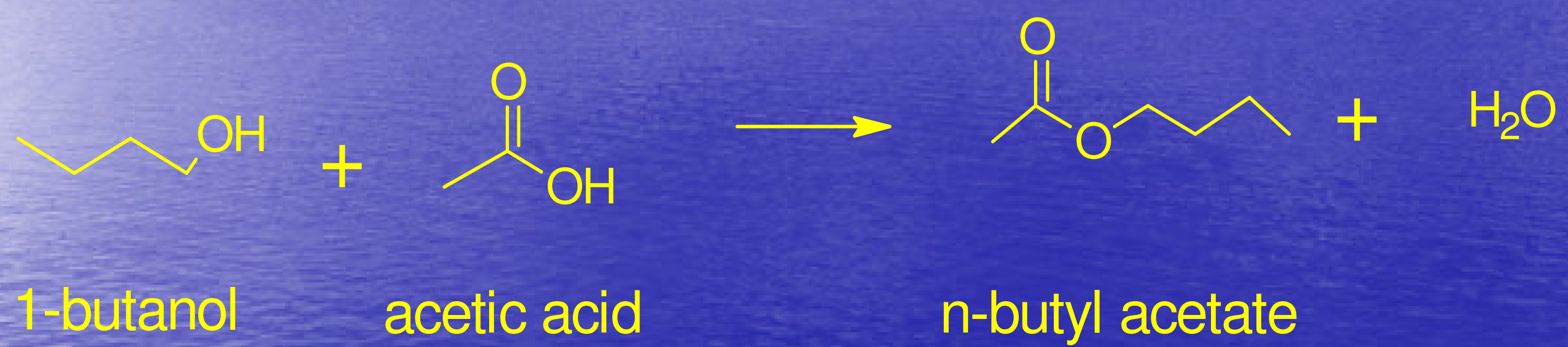
Atom Economy

- Atom Economy= $\frac{\text{MW of Product}}{\text{MW of all Reagents}} \times 100\%$

- The incorporation of as many of the atoms used in the reagents into the final product.

Atom Economy

- For Example…



- $\frac{116.15g\ C_6H_{12}O_2}{(74.12g\ C_4H_{10}O + 60.05g\ C_2H_4O_2)} \times 100\% = 86.6\%$

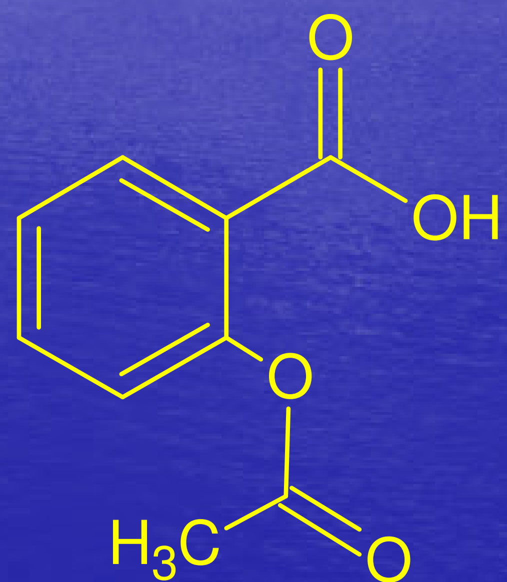
- By-Product is H_2O accounting for 18.02g

Identity of By-Product

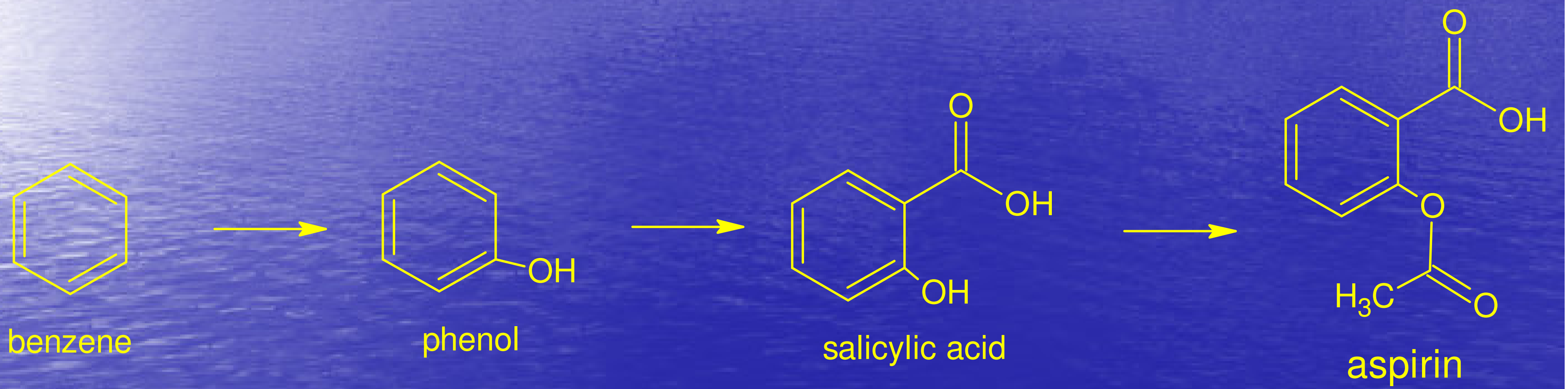
- Generate small by-products (ex. H_2O)
- By-products must be evaluated for:
  - Toxicity
  - Potential hazards (volatile, Cl_2)
  - Ease and appropriateness of Disposal (Drain, Scrubbers, Fume Hood)

A Greener Synthesis of Acetylsalicylic Acid (Aspirin)

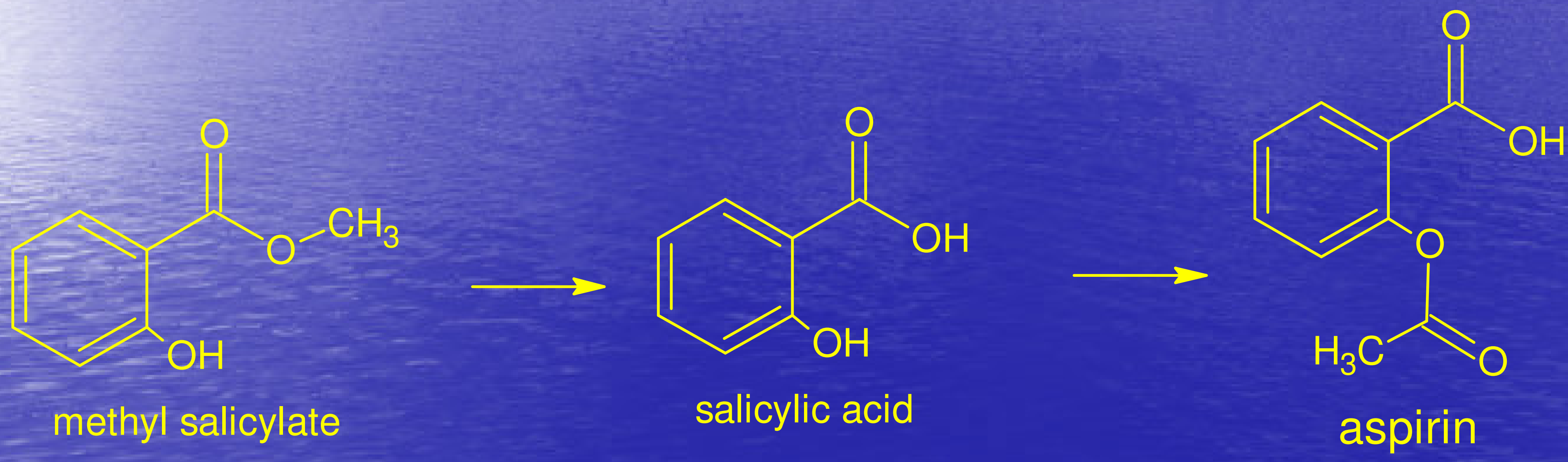
- Developed by Felix Hoffman in 1893
- Suggested adding an acetyl group to salicylic acid
- Today aspirin is the most widely used medicine of all time.



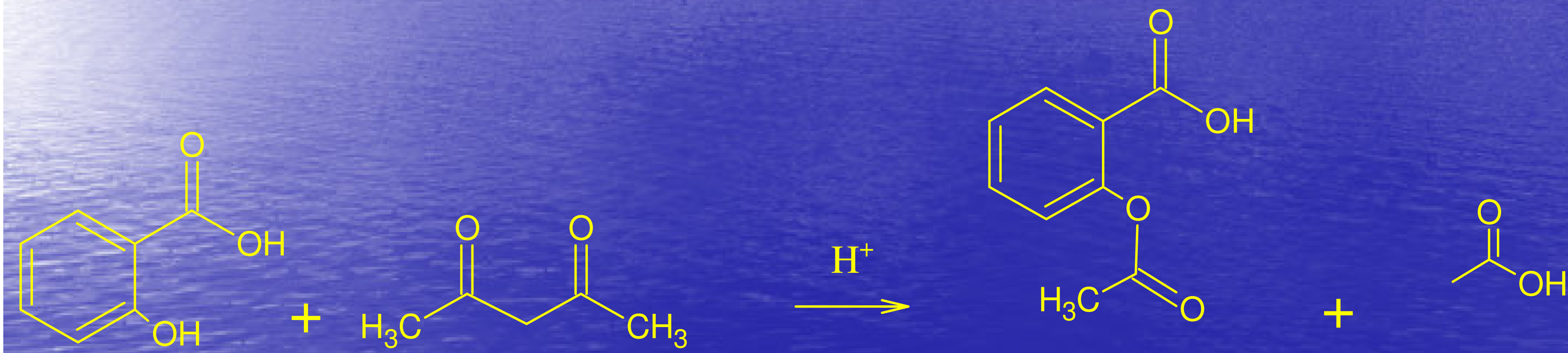
Commercial Synthesis of Aspirin



Natural Synthesis of Aspirin



Experimental Synthesis of Aspirin



salicylic acid | acetic anhydride | aspirin | acetic acid

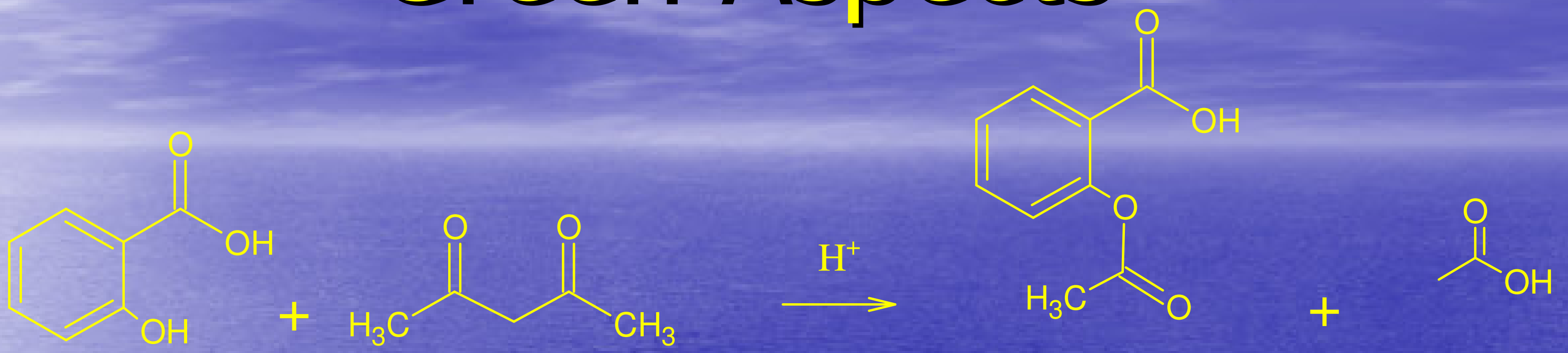
Experimental Variable

- Temperature
  - 50 ^{0}C for 15 minutes
  - 90 ^{0}C for 5 minutes
- Tested
  - Average percent yields were 20% higher at 90 ^{0}C

Experimental Procedure

- 1:3 molar ratio mixture of salicylic acid and acetic anhydride
- 3 drops of catalytic 85% phosphoric acid
- Heated in open air reflux apparatus for 5 minutes at 90 ^{0}C
- Reaction was quenched with 5 mL of H_2O (destroy excess acetic anhydride)
- Cooled in ice bath, and collected percipitate by vacuum filtration

Green Aspects



salicylic acid	acetic anhydride	aspirin	acetic acid
FW= 138.1	FW= 102.1	FW= 180.2	FW= 60.0

- Reagent made from renewable resource
- Acid catalyst
- No additional solvent
- Absence of fume hood
- Average Percent Yield= 93%
- Atom economy= 75%
- Safe by-product (Acetic Acid)
- Confirmed by IR spectroscopy, melting point, and proton NMR

Undergraduate Procedure

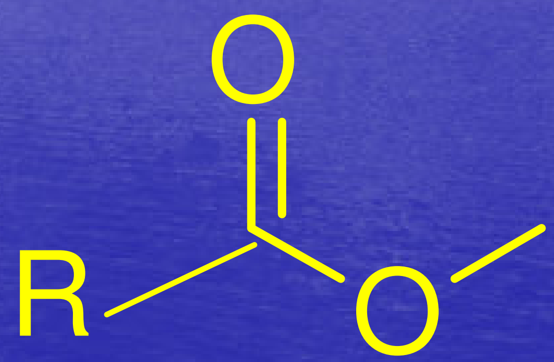
- Used optimized procedure to develop student procedure
- Facilitated undergraduate experiment
- Collected and analyzed undergraduate results

Undergraduate Lab Results

- Percent Yield range= 63% to 84%
- Average Percent Yield= 75%
- Confirmed identity by IR spectroscopy and melting point determination
- Experimental Time: 2hrs

Esters

- Pleasant scents
- Widely used
  - Preservatives
  - Additives
  - Fragrances
  - Lotions

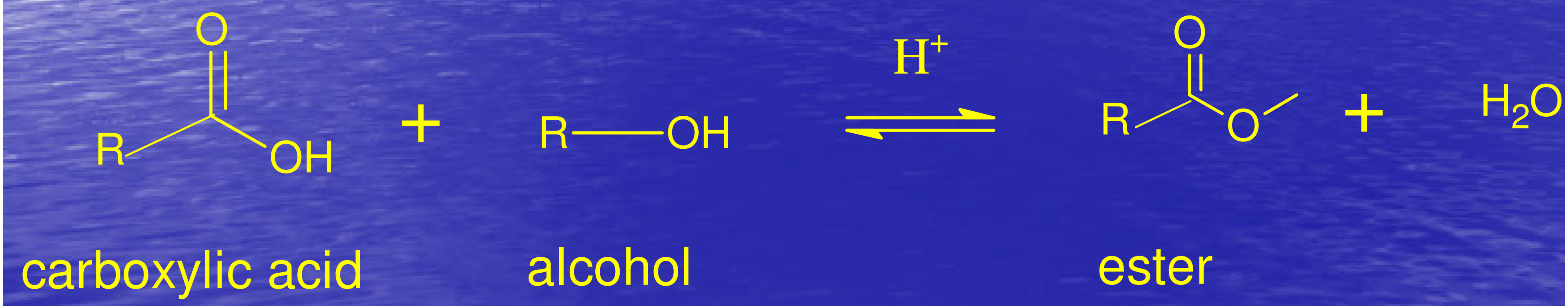


Fischer Esterification

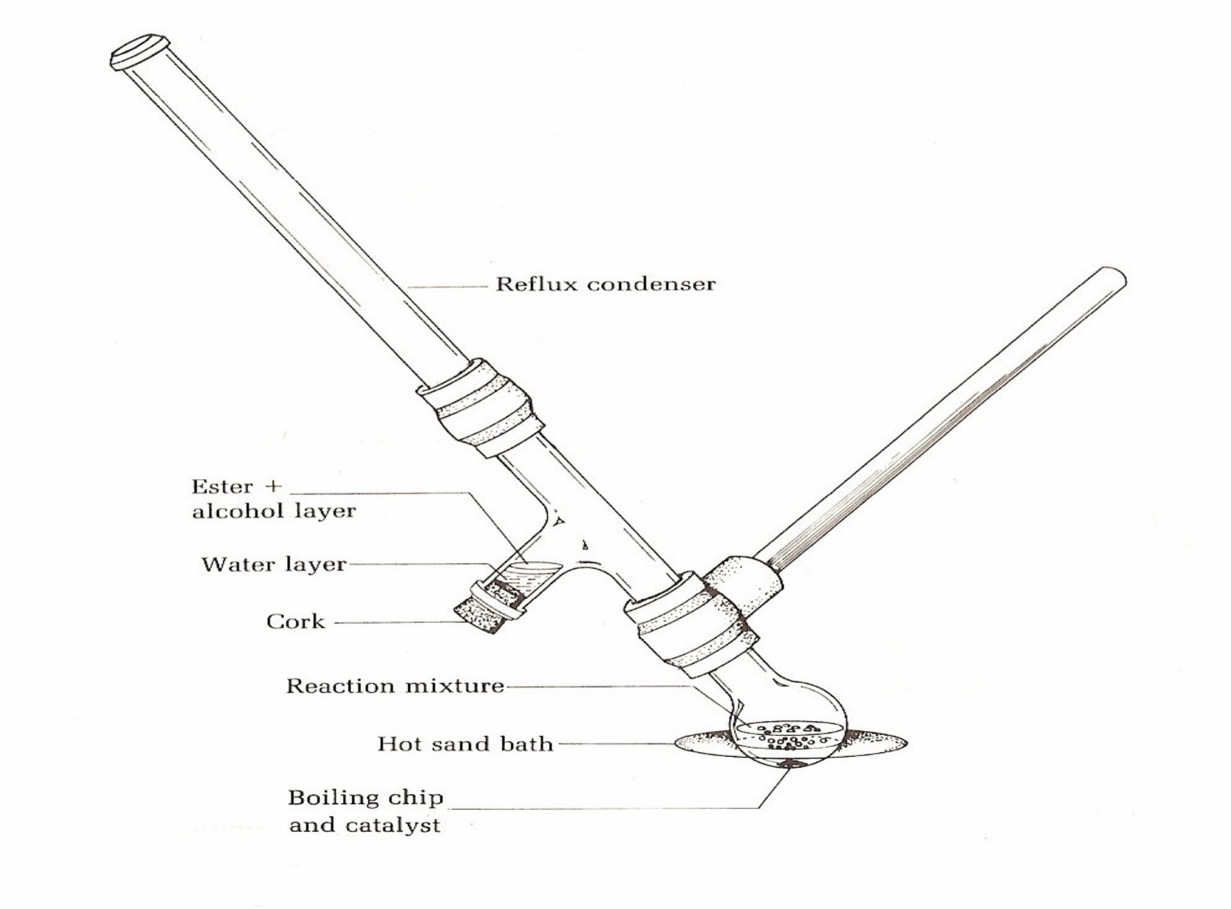
carboxylic acid alcohol ester water

Issues with Fischer Esterification

- Equilibrium Issues
- Ways to Shift Equilibrium
  1. Use excess of one reagent
  2. Remove product



Esterification by Azeotropic Distillation of Water



- Microscale azeotropic apparatus

A Greener Esterification

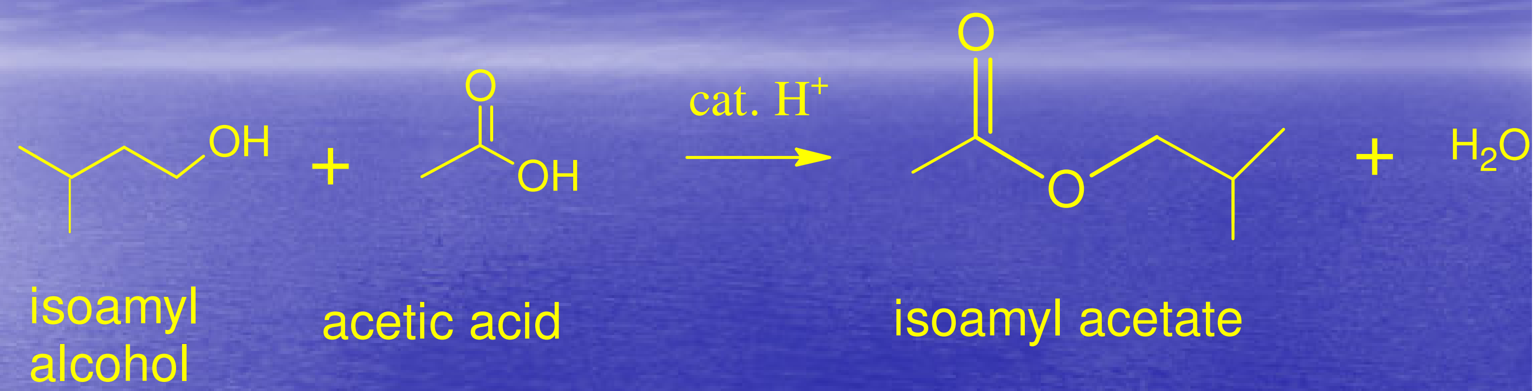
- Requirements for azeotropic distillation
  - Alcohol can not be miscible in water
  - Four carbon alcohol or larger is needed

General Procedure

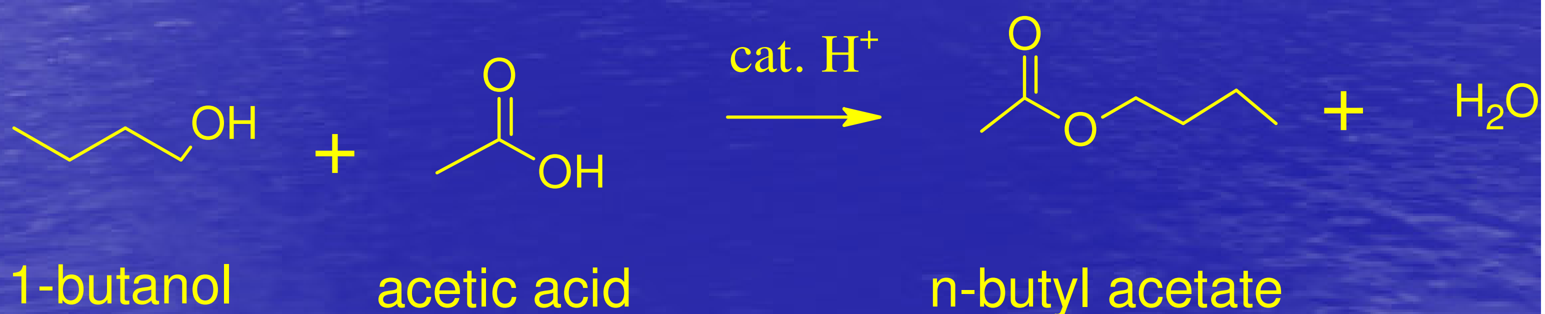
- 10 mmol carboxylic acid
- 10 mmol alcohol
- 0.20g Dowex resin beads (acid catalyst)
- Refluxed mixture in apparatus for ca. 20 minutes (until secession of growth of water layer)
- Removed resulting liquid from resin beads via pipette
- Confirmed Ester by IR spectroscopy, refractive index value, and proton NMR

5 Experimental Esterifications

- Isoamyl Acetate

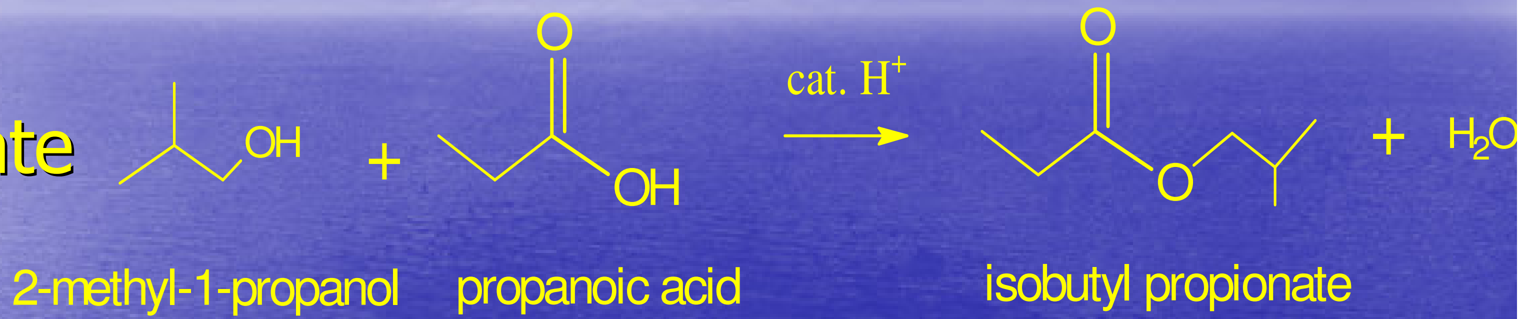


- n-Butyl Acetate

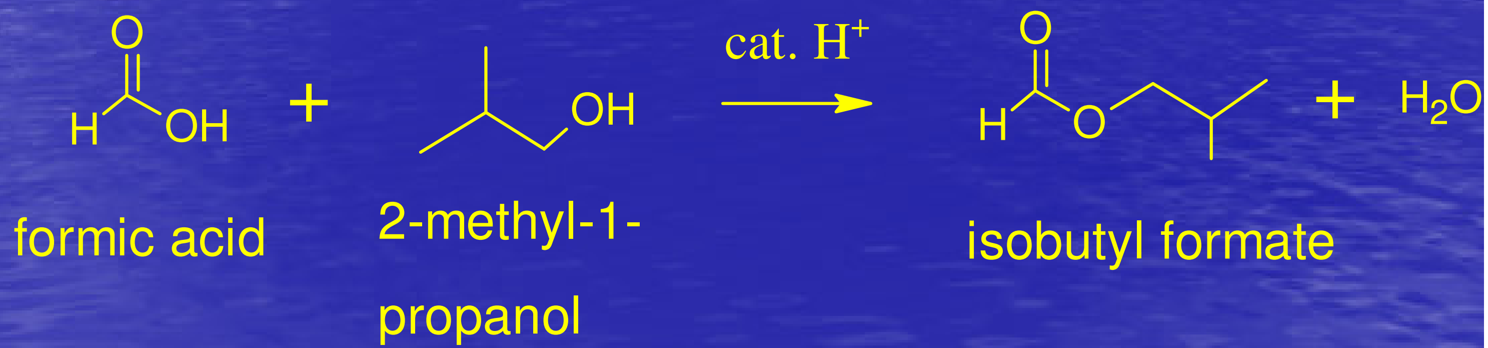


Experimental Esterifications

- Isobutyl Propionate

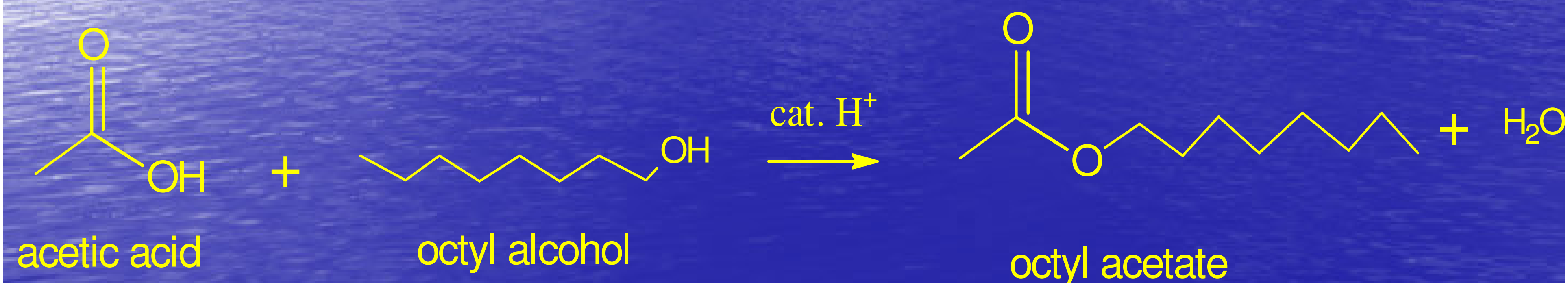


- Isobutyl Formate

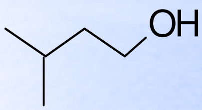
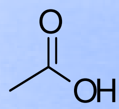
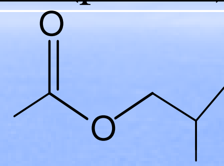
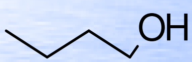
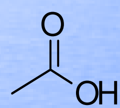
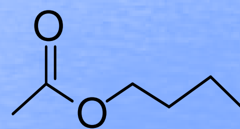
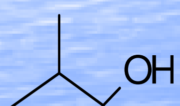
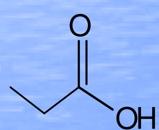
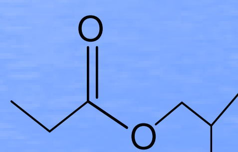
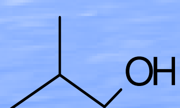
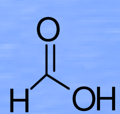
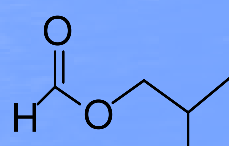
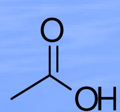
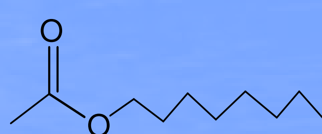


Experimental Esterifications

- Octyl acetate



Experimental Outcomes

Alcohol	Carboxylic Acid	Ester (product)	Avg. % Yield	Atom Economy	Fragrance
			89.2	87.8%	bananas
			83.0	86.6%	sour apple
			88.0	87.8%	tropical rum
			85.6	85.0%	raspberry
			80.2	90.5%	orange

Green Aspects

- Safe Reagents
- No excess of Reagents Needed
- Acid Catalyst
- Dowex Resin Beads- Recoverable & Reusable
- Solventless Reaction
- Absence of fume hood
- High Atom Economy
- Safe By-Product (H_2O)
- Pleasant scent

Ester	Atom Economy (%)
isoamyl acetate	87.8
n-butyl acetate	86.6
isobutyl propionate	87.8
isobutyl formate	85.0
octyl acetate	90.5

Undergraduate Experiment

- Organic Chemistry Lab performed esterification using the general method
- Each student performed 1 of 3 reactions as an "unknown"
  - Isoamyl acetate
  - n-Butyl acetate
  - Isobutyl propionate
- Students were asked to identify the ester and scent generated

Undergraduate Lab Results

- Percent Yield range= 62% to 81%
- Average Percent Yield= 72%
- Products were successfully confirmed by IR spectroscopy, refractive index value, and generation of expected scent

Conclusion

- Experimental and Undergraduate Data was collected and interpreted.
- Data Gives Evidence that both Aspirin and Fischer Esterification Procedures can be performed safely and effectively in an undergraduate organic lab.
- Procedural evaluations conclude that both reactions have been significantly improved for overall greenness.
- **A Win : Win Situation** is a **SUCCESS** in **Green Chemistry!** (Performing safe, efficient reactions while minimizing environmental harm)

Acknowledgements

- Special Thanks To:
  - Dr. Carl Lecher
  - Marian College and The Department of Natural and Behavioral Sciences
  - CHE 498 Group

QUESTIONS…..?