

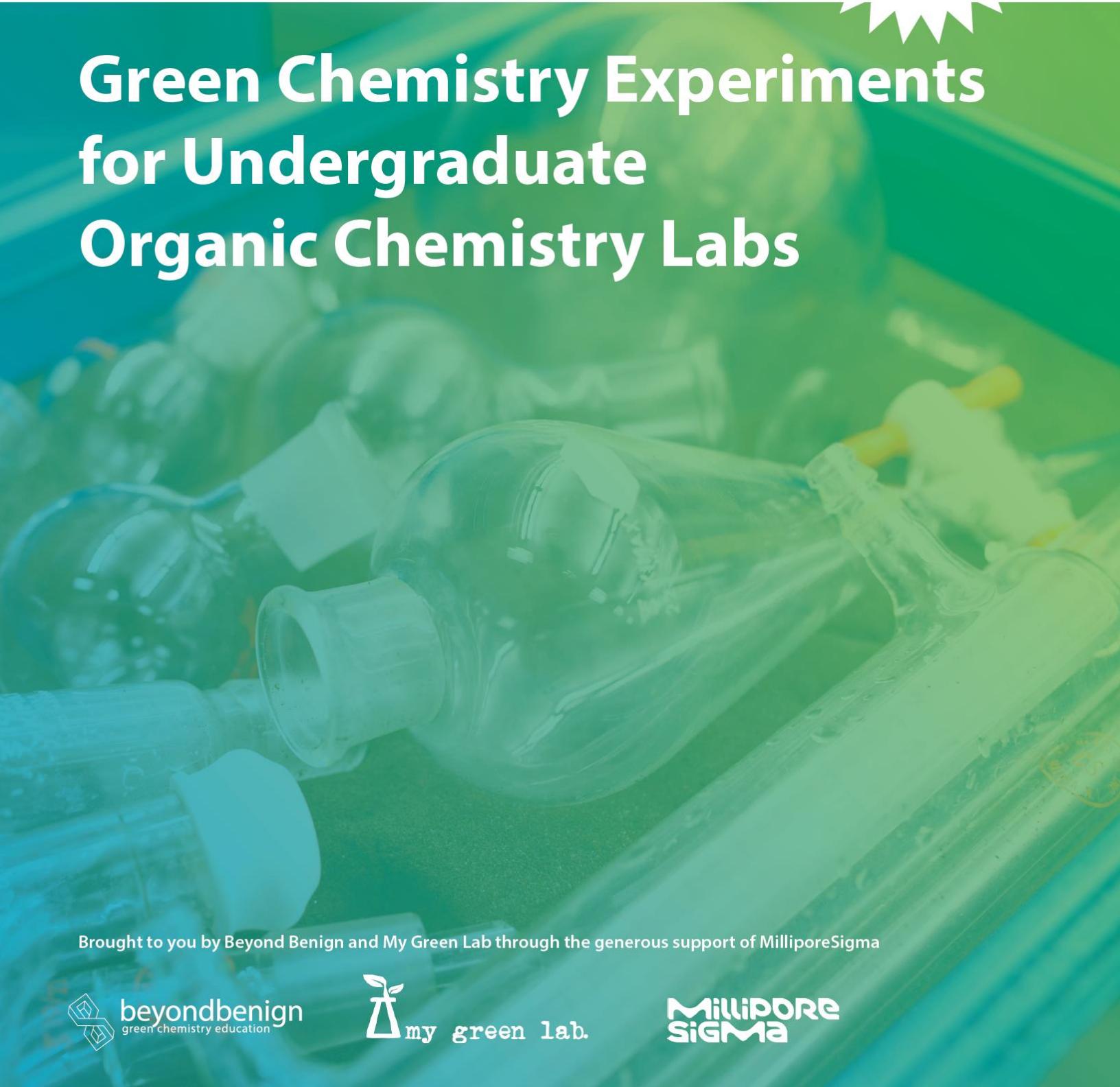


A GUIDE TO

Newly  
Revised!

v2. 2020

# Green Chemistry Experiments for Undergraduate Organic Chemistry Labs



Brought to you by Beyond Benign and My Green Lab through the generous support of MilliporeSigma



## Contents

Acknowledgements .....	3
About this Guide .....	4
Green Chemistry: Principles and Lab Practices.....	7
What is Green Chemistry?.....	7
Life- Cycle Impacts of Chemicals – ACT Label.....	9
The 12 Principles of Green Chemistry – A Primer for This Guide .....	10
Green Chemistry Principles & Laboratory Safety .....	18
Green Chemistry Lab Practices .....	19
Solvent Substitution Resources .....	19
Pfizer Solvent Selection Tool .....	19
GlaxoSmithKline (GSK) Solvent Selection Guide.....	21
American Chemical Society Green Chemistry Institute Pharmaceutical Roundtable Solvent Selection Guide and Solvent Selection Tool.....	22
CHEM21 selection guide of classical- and less classical-solvents .....	23
Beyond Benign Solvent Guide Magnet.....	25
Alternatives to Dichloromethane in Chromatography .....	26
Biorenewable Dipolar Aprotic Alternative – Cyrene™ .....	28
Reagent Selection Guides .....	29
ACS GCI Reagent Guides.....	29
GlaxoSmithKline (GSK) Reagent Guides .....	30
Greener Laboratory Techniques.....	31
Distillation: Simple and Fractional .....	31
Chromatography: TLC and Column.....	32
Extraction.....	33
Reaction Selection Resources for Organic Chemistry Laboratories.....	35
Organic Reactions under Aqueous or Solvent-Free Conditions .....	35
Incorporating Research into the Organic Laboratory Curriculum .....	37
Reactions Selected for Assessment .....	37
Methodology used for Quantitative and Qualitative Assessment for this Guide .....	38
Green Chemistry Metric: DOZN™ 2.0 .....	39
DOZN™ 2.0 Access and Scoring .....	43
DOZN™ 2.0 Scoring Example.....	44

## Acknowledgements

This resource guide has been developed through a collaboration of [Beyond Benign](#), [MilliporeSigma](#), [My Green Lab.](#), and a network of chemistry faculty to create a guide with the most up to date resources for practicing green chemistry in laboratory settings. All experiments are adapted directly from literature publications and have not been created or are not owned by any of the organizations that created this guide. Some text included in the introduction and teaching assistant guide and select example quiz questions have also been adapted directly from the original publication introduction, discussion, and supporting information. Full credit is given to the author and journal of each, and references are provided accordingly with notes about additional information contained within the supporting information for the publication that may be useful to instructors or teaching assistants.

## Academic Contributors



The following is an alphabetic list of academic contributors, and their institutional affiliations, who were consulted about content for this guide. Some through the [Green Chemistry Commitment \(GCC\)](#) program fostered by Beyond Benign. We thank all the academic contributions for actively transitioning their teaching and research labs to greener procedures and for sharing their resources to advance green chemistry education in higher education. Throughout the guide, the GCC logo will highlight labs developed, contributed, utilized or recommended by GCC signers.

Dr. Samson Alayande, First Technical University	Dr. Aaron Amick, Washington College
Dr. Brad Andersh, Bradley University	Dr. Loyd Bastin, Widener University
Dr. George Bennett, Millikin University	Dr. Daniel Berger, Bluffton University
Dr. Greg Boyce, Florida Gulf Coast University	Dr. Jason Cross, Drexel University
Dr. Deborah Bromfield Lee, Florida Southern College	Professor Irvin J. Levy, Simmons University
Dr. Andy Dicks, University of Toronto	Dr. Dalila Kovacs, Grand Valley State University
Dr. Tara Kishbaugh, Eastern Mennonite University	Dr. Ryan Trovitch, Arizona State University
Dr. David A. Laviska, Seton Hall University	Dr. Steven Wathen, Siena Heights University
Dr. Karen Matchett, Grand Valley State University	Dr. Akash Mehta, South Dakota State University
Dr. Matthew Mio, University of Detroit Mercy	Dr. Jane Wissinger, University of Minnesota
Dr. Jessica Tischler, University of Michigan – Flint	Dr. Michael Young, The University of Toledo
Dr. Haim Weizman, University of California, San Diego	Dr. David Vosburg, Harvey Mudd College
Dr. Susan Mitroka-Batsford, Worcester State University	



### *About Beyond Benign*

Beyond Benign is a non-profit organization dedicated to green chemistry education. Beyond Benign disseminates green chemistry concepts and best practices globally to science educators, scientists and the public at large through our education programs that are designed to teach and demonstrate Green Chemistry Principles across the education continuum, K-20+. Beyond Benign would like to thank Amy Cannon, Alicia McCarthy, Derrick Ward, Irv Levy and Natalie O’Neil for their contributions to this guide.

### *About My Green Lab*

My Green Lab works to reduce the environmental impact of laboratories by fostering collaboration between scientists, students, sustainability directors, environmental health and safety personnel, procurement, vendors, and regulatory agencies. A 501c3 non-profit, My Green Lab has set standards for labs across North America with a Green Lab Certification program, and for products sold into labs through work with the EPA, ENERGY STAR®, and creation of the ACT Label. My Green Lab would like to thank Erika Daley and Rachael Relph for their contributions to this guide.

### *About MilliporeSigma*

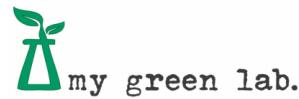
MilliporeSigma is a leader in life science, with a purpose to solve the toughest problems in life science by collaborating with the global scientific community – and through that, aims to accelerate access to better health for people everywhere by providing scientists and engineers with best-in-class lab materials, technologies, and services. With the 2015 combination of EMD Millipore and Sigma-Aldrich, there is now a broad portfolio of 300,000 products available, an expanded global footprint and an industry-leading eCommerce platform at [SigmaAldrich.com](http://SigmaAldrich.com). MilliporeSigma is dedicated to making research and biotech production simpler, faster and safer. MilliporeSigma would like to thank Dr. Ettigounder Ponnusamy, Fellow & Global Manager, Green Chemistry and Brylon Denman, Green Chemistry Intern for their DOZN™ 2.0 calculation contributions to this guide.

### *About this Guide*

This guide has been developed as a partnership between Beyond Benign, My Green Lab, and MilliporeSigma, three organizations committed to promoting the adoption of green chemistry into chemistry curricula in higher education. We have collaborated to create this guide with the hope that green chemistry will be adopted into undergraduate organic chemistry laboratories and beyond. The organic chemistry laboratory is an opportunity to give students first-hand experience with reactions and techniques central to organic chemistry. Introducing green chemistry into the curriculum maintains fundamentals and rigor while reducing hazards and waste in laboratory courses. For the health of our planet and our people, we believe it is important to train the next generation of chemists to think critically about their chemistry and explore ways to reduce the health and environmental impacts of the molecules they are designing.

As such, this guide contains more than experimental procedures. The Green Chemistry: Principles and Lab Practices can serve as both a primer for this guide and as a resource bank for practicing green chemistry in any laboratory setting to reduce human health and environmental impacts.

In this guide you will find alternatives to some of the most common undergraduate organic chemistry laboratory experiments. Each experiment begins with a discussion comparing the traditional method and



the greener method. Special attention is given to highlighting the reduced health and environmental impacts of the materials used and waste generated by the green chemistry method. The guide utilizes the [green chemistry metric, DOZN™ 2.0](#), which uses a quantitative method to recognize and assess the risks of hazards in a chemical reaction. In addition, each experiment has a detailed protocol and discussion questions for students that can be incorporated into the lesson and that gives students practice utilizing green chemistry principles, tools and metrics.

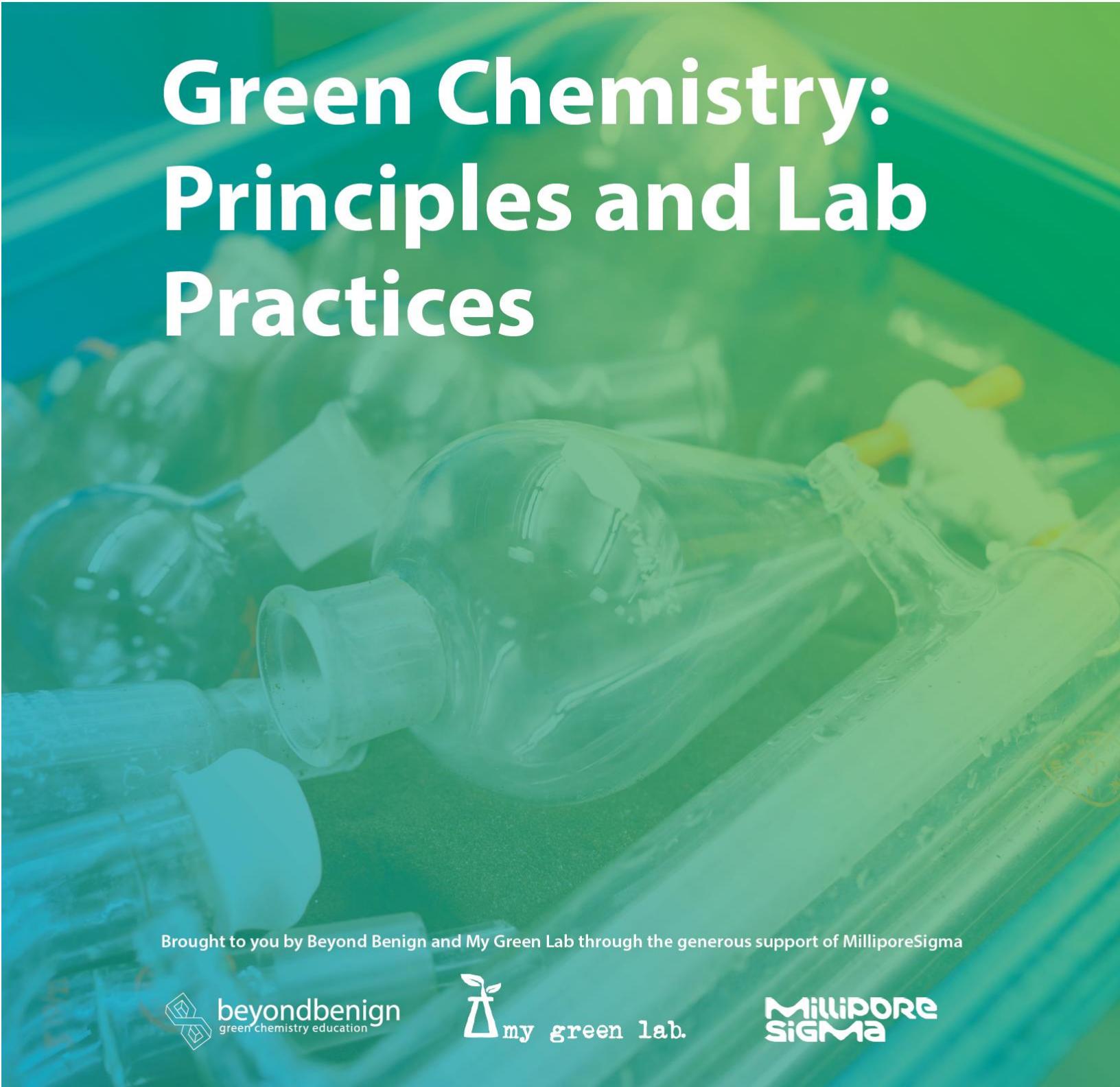
This guide could be used to substitute a single experiment or to design a whole new curriculum. To support this, the guide provides multiple pathways for adopting greener labs and points faculty members to options that can be tailored to suit the needs of their own department and courses. We encourage you to use this guide as a starting point and build upon this framework to suit the needs and unique format of your teaching laboratory.

We want to hear your feedback about this resource! Contact us at My Green Lab ([info@mygreenlab.org](mailto:info@mygreenlab.org)) or at Beyond Benign ([info@beyondbenign.org](mailto:info@beyondbenign.org)) if you have questions or comments. You will only be contacted by us should we update the guide, have questions about how you are using the guide, or have a need to communicate relevant information about green chemistry experiments for organic chemistry labs.



Green Chemistry Experiments  
for Undergraduate  
Organic Chemistry Labs

# Green Chemistry: Principles and Lab Practices



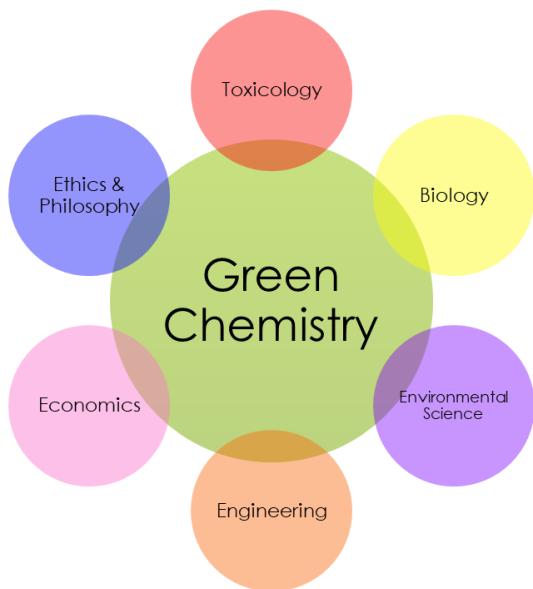
Brought to you by Beyond Benign and My Green Lab through the generous support of MilliporeSigma



## Green Chemistry: Principles and Lab Practices

### What is Green Chemistry?

Green chemistry is not a sub-discipline of chemistry – it is an umbrella philosophy/approach that encompasses not only all divisions of chemistry, but virtually all divisions of science, business, and arts. Examples of interconnected divisions of green chemistry are shown on the left.



Do not be overwhelmed – you do not need to be an expert in each area to be successful in using and applying green chemistry in practice. Collaboration is key! Partnerships and working with colleagues and other departments to help each other make research and science as efficient and sustainable as possible is encouraged.

Thinking holistically and looking at problems with the big picture in mind, especially through the lens of sustainability, is an increasingly valuable skill to have in the modern workplace. Many companies have energy, waste, hazard reduction, and other aggressive

sustainability goals in place and are seeking scientists that know how to collaborate to implement such measures. Learning to use green chemistry tools and thinking is therefore a valuable skill for the next generation of scientists to develop. So, let's get started!

Green chemistry is a set of guidelines for evaluating laboratory procedures and chemical products that looks to minimize adverse health, safety and environmental impacts. Though it seems like it is a sub-discipline of chemistry, green chemistry actually requires an interdisciplinary view of material and product design, applying the principle that it is better to consider waste and hazard prevention options during the design and development phase, rather than disposing, treating and handling waste and hazardous chemicals after a process or material has been developed.

*Green Chemistry is the **design of chemical products and processes** that reduce and/or eliminate the **use or generation of hazardous substances**<sup>1</sup>*

Green chemistry is an opportunity to introduce innovative solutions to chemical problems and apply sustainability to molecular design. Chemists can design products and processes that have reduced impacts on humans and the environment and therefore create sustainable chemical building blocks for materials and products in our society.

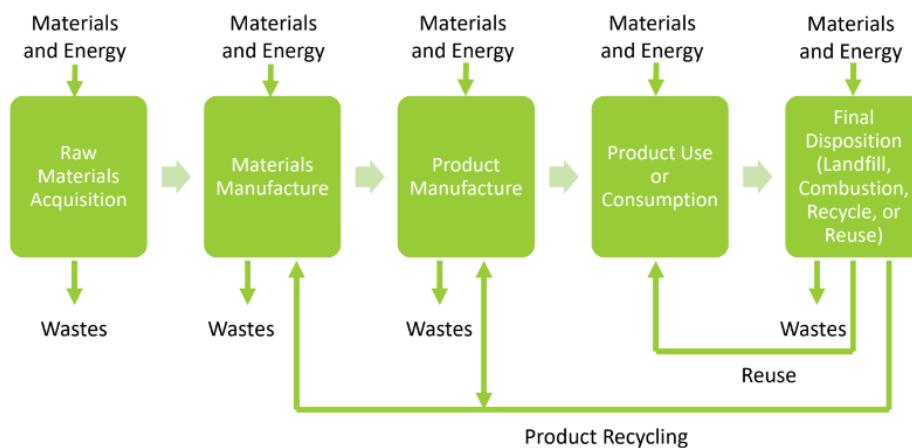
---

1. Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: New York, 1998.

In order to apply the principle that it is better to consider waste and hazard prevention during design, rather than disposing, treating and handling waste after a has been developed, we need to think beyond the bounds of the reaction or process in front of us. We need to consider:

- the raw materials that are being used, how they were made and what hazards were generated in their production
- the materials used and waste generated (including chemicals, heat, solid waste) in the creation of a chemical product
- the ancillary materials needed to use a product and the fate of the product in the environment (e.g. pharmaceuticals)
- the disposal of all materials and wastes used and generated in making the product

This big-picture view of a product is called a life-cycle assessment. The major stages in a products lifecycle will be Materials Extraction, Manufacturing, Distribution, Usage, and End-of-Life. Each product will have many different factors that determine a material's impact at each of these stages.



**Figure 1.** Recreated from: Guidance on Life-Cycle Thinking and Its Role in Environmental Decision Making, Sustainable Materials Management Coalition.<sup>2</sup>

Learning to adopt life-cycle thinking does not happen overnight. The twelve principles of green chemistry, which we will discuss in detail below can be thought of as a framework for evaluating the life-cycle impacts of a chemical process or product. They challenge chemists to consider where their raw materials come from and the kinds of materials used, and wastes generated in a process.

---

2. Guidance on Life-Cycle Thinking and Its Role in Environmental Decision Making, Sustainable Materials Management Coalition, March 2014 [<https://www.michaeldbaker.com/wp-content/uploads/2014/03/Guidance-on-Life-Cycle-Thinking-031014.pdf>].

## Life-Cycle Impacts of Chemicals – ACT Label

To aid scientist in considering some of the life-cycle impacts of the chemicals they purchase, the ACT label combines information about the impact of manufacturing, using, and disposing of a chemical and its packaging. By emphasizing accountability, consistency, and transparency (ACT) during different lifecycle phases, ACT labeling is designed to make it easy to compare and choose more sustainable products. Presented as an eco-nutrition label for the product, the results are reported in a virtual label where the lower the number, the lower the environmental impact. To ensure integrity, products with the ACT label have undergone an extensive audit by two independent third-parties. Not all products have this label; those that do can be found at [act.mygreenab.org](http://act.mygreenab.org). Because transparency around the lifecycle of a product makes it easier to choose the most benign option from all perspectives, look for the ACT label in conjunction with the other resources provided in this guide.

<b>ACT.</b> Accountability, Consistency, Transparency. The Environmental Impact Factor Label	
Product Name	
Manufacturing Location	
<b>Manufacturing</b>	
Manufacturing Impact Reduction	
Renewable Energy Use	
Responsible Chemical Management	
Shipping Impact	
Product Content	
Packaging Content	
<b>User Impact</b>	
Energy Consumption	
Water Consumption	
Lifetime Rating	
<b>End of Life</b>	
Packaging	
Product	
<b>Environmental Impact Factor</b>	
Label Valid Through	
My Green Lab  <a href="http://mygreenlab.org">mygreenlab.org</a>	
<small>**Energy and water consumption reported as daily values, all other values on a scale of 1-10: 1 indicates the least environmental impact and 10 indicates the greatest.</small>	

## The 12 Principles of Green Chemistry – A Primer for This Guide

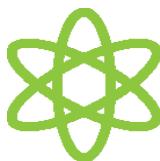
As discussed above, the twelve principles of green chemistry provide a framework for evaluating and minimizing the life-cycle impacts of a product or process. In addition to setting best practices in how to minimize these impacts, some principles also incorporate tools for calculating efficiency or minimizing waste. Each of the experiments in this guide will align with one or more of the 12 Principles of Green Chemistry – some experiments align with only one, while some experiments align with several. Every principle except for real-time monitoring to prevent pollution is represented in this guide. As we review the 12 Principles below, we will highlight an example of where each principle applies to experiments in this guide when possible.



### *Principle 1 – Prevent Waste*

Many chemical reactions produce waste, either as liquid waste or as solid waste. For decades we have been working under the premise that it was acceptable to generate waste because we could treat it, dilute it or incinerate it and release it back into the environment. But waste is expensive to manage and to treat, it introduces risks to the people managing and disposing it, and there is always a risk that it will be released into the environment where it is much more difficult to clean up and can have long term impacts to human and environmental health.

Principle 1– Prevent Waste is a best practice that encourages chemists to minimize the amount of waste that is generated to avoid having to manage its downstream impacts. It is better to avoid a problem than try to fix it later. To help scientists evaluate how much waste a process generates there are a couple tools available. E-factor is a measure of the total amount of waste generated in a process divided by the mass of the desired product. The lower the E-factor, the less waste generated and the greener the process. Process Mass Intensity (PMI) is another tool favored by pharmaceutical makers that is a ratio of the mass of all starting materials (reactants and solvents) divided by the mass desired product. Similarly, the lower the PMI, the greener the reaction.



### *Principle 2 – Maximize Incorporation of Materials; Atom Economy*

In many regards, Principle 2 – Maximize Incorporation of Materials (Atom Economy), can be thought of as a strategy to achieving Principle 1. Materials that do not get incorporated into the final product end up as waste. Traditionally, we have used the concept of “yield” to measure efficiency of a reaction by calculating the actual mass obtained of the desired product divided by the theoretical mass obtainable based on the reaction stoichiometry. This does not take into account the masses of other materials needed for the reaction.

The green chemistry approach is to use atom economy which is calculated similarly to yield but instead uses the molecular weight of the desired product divided by the molecular weight of all the starting materials. As a simple example, consider the reaction:  $\text{CH}_4(\text{g}) + 2\text{O}_2(\text{g}) \Rightarrow 2\text{H}_2\text{O}(\text{g}) + \text{CO}_2(\text{g})$  where 32 grams of methane burns completely to form 66 grams of water. The percent yield of water would be calculated by first converting the 32 grams of methane into moles of methane (2 mol) and using the reaction stoichiometry to calculate moles of water (4 mol). The moles of water are then converted into grams of water to get 72 grams. The percent yield is then the 66g obtained, divided by the 72 grams theoretically produced to give a 92% yield. The atom economy for the same reaction is calculated by taking the molecular weight of the water (18 g \* 2 moles = 36 g) and dividing it by the molecular weights of all starting materials (16 g + 2\*32 g = 80 g) to get an atom economy of 45%. The atom economy gives a much more useful look at how starting materials are being incorporated into the final product. In this guide, there 100% atom economy is achieved for the Diels-Alder transformation.



#### *Principle 3 – Use and Generate Less Toxic Materials; Less Hazardous Chemical Syntheses*

A major part of designing more benign chemistries is embodied in Principle 3: To Use and Generate Less Toxic Materials. Many of the chemicals we use have various health and environmental hazards from oxidizers to carcinogens. Weighing each of these hazards and comparing them across different hazard types can be tricky. Many organizations have developed Greener Alternative Selection Guides to help make these choices easier. Using less toxic materials minimizes the risk of exposure or release of those materials during manufacturing, transport and use by you. It also helps to reduce the generation of hazardous waste when you are done with the materials, further supporting Principle 1.



#### *Principle 4 – Design Safer Chemicals*

Designing Safer Chemicals, Principle 4, can be challenging. It requires an understanding of how chemicals are metabolized in the body and what their fate is in the environment – an area of science where data is often lacking. As we begin to learn more about the long-term impacts of acutely toxic and bioaccumulative substances, it is imperative that we partner with toxicologists and environmental scientists to understand how a product will degrade in the human body and in the environment. In this guide, the polymerization reaction gives the greener approach by creating a biodegradable polymer.



### *Principle 5 – Safer Solvents and Auxiliaries*

In the same way that Principles 2 and 3 support waste prevention, Principle 5, Minimizing Auxiliary Substances, also supports the reduction of waste. During many chemical transformations, solvents are needed to aid in the chemistry or are used to separate products from starting materials. Solvents and auxiliary substances end up as waste and contribute greatly to the life-cycle impacts of a chemical process. Energy and other resources are needed to make, and transport solvents and energy is often expended in removing solvents from a final product as well. By minimizing the use of auxiliary substances, you can not only prevent waste at the end, but minimize impacts from the beginning of the life-cycle as well.

Luckily, there are several strategies today for reducing the use of auxiliary substances like supercritical fluids, solventless chemistries, aqueous chemistries, and immobilization techniques. In this guide, reactions in water are highlighted along with a Grignard reaction in water and solventless approaches.



### *Principle 6 – Minimize energy use; Design for Energy Efficiency*

As we just discussed in Principle 5, energy is often needed to separate solvents from products. Principle 6, Minimize Energy Use, seeks to minimize energy use in all parts of a chemical process. If you think about it, energy is needed to heat or cool a reaction, it is needed for separations, condensations, purifications, and in a variety of other ways.

In green chemistry, we look for ways to conduct experiments at ambient temperatures and pressures (or closer to ambient) so that energy needed to create high or low pressures or temperatures can be minimized.



### *Principle 7 – Renewable Feedstocks*

Since the 1800's scientists have been making chemicals from petroleum extracts and in today's market, many common chemicals are derived from petroleum. Widely understood to be a non-renewable resource, petroleum has become the major source of chemicals for the laboratory. Principle 7, Renewable Feedstocks, recognizes that continued use of chemicals from a non-renewable feedstock like petroleum is not sustainable.

Luckily today there are a variety of new processes and chemistries being developed to create chemicals from renewable feedstocks like algae, sugar cane and other renewable resources. Chemicals from these sources are becoming more widely available. In this guide, The Esterification Reaction uses vegetable oil to make biodiesel.



### *Principle 8 – Reduce Derivatives*

In chemistry it is very common to use protecting groups to avoid unwanted chemistry happening at a reactive site. Although very practical, protecting groups require additional chemistry, and as a result energy and resources, to put on and to take off. Principle 8, Reduce Derivatives, looks to minimize the use of additional materials by avoiding the creation of derivatives and the use of protecting groups. But how do you do this? One common way is with enzymes and biological processes to make transformations and there are a growing number of examples in the literature of where this has been done.



### *Principle 9 – Use catalysts*

Catalysts, or substances that can accelerate the rate of a reaction without being changed in the reaction, are one of most important tools in the green chemistry tool kit. Catalysts can enable reactions to be done under lower temperatures, they allow selective modifications and can reduce the number of steps in a synthesis or the quantity of reagents used, and as a result have higher atom economy and generate less waste.



### *Principle 10 – Design for Degradation*

Related to Principle 4 to Use and Design Safer Chemicals, Principle 10, to Design for Degradation, focuses on designing products that readily degrade and do not persist and accumulate in the environment. It is important to design chemicals that are effective but will not have an adverse effect after they have served their purpose. Whether a substance degrades by hydrolysis, photolysis, or other chemistry, it is also important to consider the toxicity of the degradation products to ensure a benign product doesn't turn into something not benign. As with Principle 4, it is important that chemists work with toxicologists and environmental scientists to understand what motifs will have an adverse effect at their end of life. In this guide, The Polymerization Reaction greener alternatives create biodegradable polymers.



### *Principle 11 – Real-Time Monitoring to Prevent Pollution*

Real-Time Monitoring of Chemical Reactions, as encouraged through Principle 11, real-time feedback in chemical reactions allows chemists to detect undesirable chemicals and adjusted the reaction conditions to minimize their creation. Based on the premise that “you can’t control what you can’t measure” real-time monitoring of chemical processes is an important technique, particularly in large-scale chemical processes. The development of real-time monitoring typically falls under the subdiscipline of process analytical chemistry and is not covered in this guide.



### Principle 12 – Accident Prevention

Principle 3, to use and generate less toxic materials, which is closely connect to Principle 12, Accident Prevention. In an experiment, when a hazard is present, you introduce various controls to reduce the risk of exposure to or harm from that hazard. These controls might include personal protective equipment like gloves or lab coats; or they might include engineering controls like a fume hood, active cooling, or maximum reaction volumes. Although these controls are there to help reduce risk, they can fail. And they add to the total cost of doing the experiment. When feasible, chemists should design experiments to use and generate substances that have the lowest health, safety and environmental impacts so risk of accidental expose or harm. In this guide, there are 12 experiments designed to generate less hazardous waste for safer laboratories.

### Additional Green Chemistry Readings and Resources

1. Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: New York, 1998.
  - This book provides the first introductory treatment of the design, development, and evaluation processes central to Green Chemistry. As a comprehensive textbook, it takes a broad view of the subject and integrates a wide variety of approaches. Topics include alternative feedstocks, environmentally benign syntheses, the design of safer chemical products, new reaction conditions, alternative solvents and catalyst development, and the use of biosynthesis and biomimetic principles. It introduces new evaluation processes that encompass the complete health and environmental impact of a synthesis, from the choice of starting materials to the final product. Throughout, the text provides specific examples that compare the new methods with classical ones.
2. [Green Chemistry University Curriculum](#)
  - The Yale-UNIDO University Curriculum is a semester long course developed in collaboration with Beyond Benign. The curriculum was developed as part of the [Global Green Chemistry Initiative \(GGCI\)](#), a joint initiative between the Center for Green Chemistry and Engineering at Yale and the United Nations Industrial Development Organization (UNIDO), and was funded by GEF (Global Environment Facility). This free open-access adaptable course is designed for undergraduate students and teaches:
    - (i) how the principles of green chemistry can help resolve global human health and environmental issues
    - (ii) how green chemistry functions
    - (iii) how it is implemented
  - Preview all the curriculum has to offer and ways to utilize it by [viewing the webinar](#)

3. [Green Chemistry Education Webinar Series](#)

- The Green Chemistry Education Webinar Series hosted by the [Green Chemistry Commitment](#) highlights relevant topics for chemistry educators and students to incorporate green chemistry into their courses, labs and programs. The webinars are open to the community and are recorded and posted for access following the live webinar. Access the webinar archive for 31 past webinar recordings.

4. [Green Chemistry Higher Education Curriculum](#)

- Beyond Benign develops and disseminates curriculum that is open access and can be downloaded directly from the website. The curriculum and resources are licensed under a Creative Commons Attribution-Noncommercial. This license allows others to adapt, remix, tweak, and build upon the work non-commercially. Many of the resources are continued from Green Chemistry Commitment signers.

5. [The American Chemical Society Green Chemistry Institute](#)

- The American Chemical Society (ACS) flagship Green Chemistry Institute convenes the global chemistry community to catalyze innovative thinking, facilitate critical conversations, and communicate the core values and benefits of green and sustainable chemistry and engineering. There are many resources within this guide from the ACS Pharmaceutical Roundtable and many more [resources as well as opportunities for students and educators](#) are available.

6. [Green Chemistry Challenge Awards](#)

- The Green Chemistry Challenge Awards promote the environmental and economic benefits of developing and using novel green chemistry. These prestigious annual awards recognize chemical technologies that incorporate the principles of green chemistry into chemical design, manufacture, and use. The Environmental Protection Agency (EPA) Office of Chemical Safety and Pollution Prevention sponsors the Green Chemistry Challenge Awards in partnership with the American Chemical Society Green Chemistry Institute and other members of the chemical community including industry, trade associations, academic institutions, and other government agencies.
- Introduce your students to the Green Chemistry Principles with cases that are rich in many areas of chemistry, lending themselves to discussion in courses such as general chemistry, organic, inorganic, biochemistry, polymer, environmental, industrial, toxicology and chemistry for non-majors through the [Real–World Cases in Green Chemistry Volume II](#).

7. [The Periodic Table of the Elements of Green and Sustainable Chemistry](#)

- In celebration of the 150th anniversary of the Periodic Table of the Elements, a new metaphorical construct has been assembled to illustrate the “elements” that will be crucial on the path to a sustainable future. This is the basis of “The Periodic Table of the Elements of Green and Sustainable Chemistry” created by Paul

Anastas, Julie Zimmerman and the [Center for Green Chemistry and Engineering at Yale](#).

8. [Greener Alternatives Learning Center | Sigma-Aldrich](#)

- The MilliporeSigma Learning Center can help you stay at the forefront of green chemistry practices, products, and resources. The Learning Center aggregates the best and brightest papers, thought leaders and resources to connect you with best practices in green chemistry to help reduce the environmental footprint of your research.

Want to bring these principles to your lab or classroom? The following infographic describes each of the principles. The graphic was designed by [Compound Interest](#) and the [Green Chemistry Initiative at the University of Toronto](#). This student group has also created a YouTube [video series](#) around each of the principles in everyday terms and situations. [Access a copy here!](#)

## The 12 Principles of GREEN CHEMISTRY

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.

<b>1. WASTE PREVENTION</b>  Prioritize the prevention of waste, rather than cleaning up and treating waste after it has been created. Plan ahead to minimize waste at every step.	<b>7. USE OF RENEWABLE FEEDSTOCKS</b>  Use chemicals which are made from renewable (i.e. plant-based) sources, rather than other, equivalent chemicals originating from petrochemical sources.
<b>2. ATOM ECONOMY</b>  Reduce waste at the molecular level by maximizing the number of atoms from all reagents that are incorporated into the final product. Use atom economy to evaluate reaction efficiency.	<b>8. REDUCE DERIVATIVES</b>  Minimize the use of temporary derivatives such as protecting groups. Avoid derivatives to reduce reaction steps, resources required, and waste created.
<b>3. LESS HAZARDOUS CHEMICAL SYNTHESIS</b>  Design chemical reactions and synthetic routes to be as safe as possible. Consider the hazards of all substances handled during the reaction, including waste.	<b>9. CATALYSIS</b>  Use catalytic instead of stoichiometric reagents in reactions. Choose catalysts to help increase selectivity, minimize waste, and reduce reaction times and energy demands.
<b>4. DESIGNING SAFER CHEMICALS</b>  Minimize toxicity directly by molecular design. Predict and evaluate aspects such as physical properties, toxicity, and environmental fate throughout the design process.	<b>10. DESIGN FOR DEGRADATION</b>  Design chemicals that degrade and can be discarded easily. Ensure that both chemicals and their degradation products are not toxic, bioaccumulative, or environmentally persistent.
<b>5. SAFER SOLVENTS &amp; AUXILIARIES</b>  Choose the safest solvent available for any given step. Minimize the total amount of solvents and auxiliary substances used, as these make up a large percentage of the total waste created.	<b>11. REAL-TIME POLLUTION PREVENTION</b>  Monitor chemical reactions in real-time as they occur to prevent the formation and release of any potentially hazardous and polluting substances.
<b>6. DESIGN FOR ENERGY EFFICIENCY</b>  Choose the least energy-intensive chemical route. Avoid heating and cooling, as well as pressurized and vacuum conditions (i.e. ambient temperature & pressure are optimal).	<b>12. SAFER CHEMISTRY FOR ACCIDENT PREVENTION</b>  Choose and develop chemical procedures that are safer and inherently minimize the risk of accidents. Know the possible risks and assess them beforehand.

© COMPOUND INTEREST 2015; WWW.COMPOUNDCHEM.COM  
Shared under a CC Attribution-NonCommercial-NoDerivatives licence.



## Green Chemistry Principles & Laboratory Safety

The intrinsic connection between green chemistry methodologies and laboratory safety culture is clear through Principle 12 – Accident Prevention. The substances and the form of a substance used in a chemical process should be chosen to minimize the potential for chemical accidents, including releases, explosions and fires under the green chemistry framework. It should be noted that Principle 12 cannot be achieved without implementing other Green Chemistry Principles and many of the principles overlap with safety considerations.

Teaching safety is shifting away from compliance and rule following, towards requiring students to think in terms of hazard assessment and risk minimization. This approach to safety is simplified to RAMP (Recognize hazards, Asess the risks of the hazard, Minimize the risk of the hazard and Prepare for emergencies). As an instructional approach to chemical safety, RAMP is beneficial because there are many overlaps with green chemistry principles. RAMP and green chemistry are complementary to each other and the use of green chemistry metrics, such as DOZNTM 2.0, explored further in this guide is an example of recognizing (R) and assessing (A) the risks of hazards in chemical reactions. With the green chemistry framework, minimizing (M) the risks can be achieved by elimination or substitution of hazardous substances and many resources are available to provide alternatives.

## Additional Reading and Resources

1. [Safety Basics & RAMP](#)
  - American Chemical Society
2. [How to Create a Safer and More Sustainable Lab Through Green Chemistry](#)
  - American Chemical Society
3. [Identifying and Evaluating Hazards in Research Laboratories](#)
  - ACS Committee on Chemical Safety Hazard Identification and Evaluation Task Force.
4. [Transitioning to Safer Chemicals: A Toolkit for Employers and Workers](#)
  - United States Department of Labor
5. [ACS Division of Chemical Health and Safety](#)
  - Wissinger, J. Paradigm shift in approach to safety through green chemistry. 23<sup>rd</sup> Annual Green Chemistry & Engineering Conference, Reston, VA, United States, June 11–13, 2019; GCE-GSC-381. [Wissinger, J. ACS Division of Chemical Health and Safety](#)
  - Wissinger, J. Green chemistry's role in promoting safety. 256<sup>th</sup> ACS National Meeting & Exposition, Boston, MA, United States, August 19-23, 2018; PRES-9. [Wissinger, J. ACS Division of Chemical Health and Safety](#)
6. [RAMP: A Safety Tool for Chemists and Chemistry Students](#)
  - Finster, D. C., *J. Chem. Educ.*, **2020** DOI: 10.1021/acs.jchemed.0c00142



## Green Chemistry Lab Practices

### Solvent Substitution Resources

Solvents are used in large volumes in reactions and in purification techniques. However, solvents do not determine the composition of the product, nor are they active components of a formulation. In the pharmaceutical industry, around 50% of materials used to manufacture bulk active pharmaceutical ingredients are solvents. The chemical industry views solvent selection as a key component in the overall sustainability profile of a manufacturing process. To help chemists choose more sustainable solvents, a few pharmaceutical companies and institutions have developed data-rich solvent selection guides with visual aids for quick selection. All the guides use the “traffic light” system and consider the safety, occupational health, environmental, cost and industrial constraints.

From these visual aids the “greenest” solvent, having low toxicity, minimal safety concerns and little impact on the environment can be selected for specific chemical process. Each of these guides is tailored to the culture and policy of the company or institution which creates discrepancies between the solvent selection guides. *There is no universal approach to solvent selection. Solvent guides are resources that should be used by chemist to make the right choice for their specific chemistry.*

The use of safer solvents is oftentimes the ‘low hanging fruit’ for implementing Green Chemistry Principles into traditional organic chemistry experiments. There are many solvent selection guides that have been published within the pharmaceutical sector and are being used as a basis for guiding the selection of safer solvent choices for chemical reactions, extractions, and separations. The following summary provides an overview of these guides, along with guidance towards safer solvent substitution.

### Pfizer Solvent Selection Tool

Pfizer created an internal solvent selection tool<sup>3</sup> that has been widely publicized. The tool categorizes solvents based on worker safety (acute and chronic toxicity), process safety (flammability, and reactivity), and environmental and regulatory considerations. Solvents are categorized into “preferred”, “usable” and “undesirable” solvents and are also presented in a solvent replacement table that can be used to guide “greener” choices for solvents (Table 1). Through internal use of the solvent selection tool, Pfizer realized a 50% reduction in chlorinated solvent use, the reduction of undesirable ether usage by 97%, and the shifting of the use of less harmful heptane over hexane and pentane across their research division during 2004-2006.<sup>5</sup>

---

3. Dunn, P. J., et al., *Green Chemistry*, **2008**, *10*, 31–36.

**Table 1.** Pfizer solvent replacement table

Undesirable Solvent	Alternative
Pentane	Heptane
Hexane(s)	Heptane
Di-isopropyl ether or diethyl ether	2-MeTHF or <i>tert</i> -butyl methyl ether
Dioxane or dimethoxyethane	2-MeTHF or <i>tert</i> -butyl methyl ether
Chloroform, dichloroethane or carbon tetrachloride	Dichloromethane
Dimethyl formamide, dimethyl acetamide or N-methylpyrrolidinone	Acetonitrile
Pyridine	Et <sub>3</sub> N (if pyridine is used as a base)
Dichloromethane (extractions)	EtOAc, MTBE, toluene, 2-MeTHF
Dichloromethane (chromatography)	EtOAc/heptane
Benzene	Toluene

Table reproduced from Dunn, P. J., et al., *Green Chemistry*, **2008**, *10*, 31–36 with permission of The Royal Society of Chemistry.

## GlaxoSmithKline (GSK) Solvent Selection Guide

GSK has developed a solvent selection guide<sup>4</sup> for use by their medicinal chemists. This solvent guide, shown below, is a quick reference tool for practicing chemists to quickly identify solvents of concern. The guide is supported by a table which identifies the areas of concern in the following categories: waste, environmental impact, health hazards, flammability and explosion hazard, reactivity and stability, life-cycle score and a legislation flag that alerts the user of any regulatory restrictions. The complete guide provides different levels of detail depending on the requirements by the user and the application.

### GSK Solvent Selection Guide

	Few issues (bp°C)	Some issues (bp°C)	Major issues
Chlorinated	....before using chlorinated solvents, have you considered TBME, isopropyl acetate, ethyl acetate, 2-Methyl THF or Dimethyl Carbonate?		Dichloromethane ** Carbon tetrachloride ** Chloroform ** 1,2-Dichloroethane **
Greenest Option	Water (100°C)	Ethanol/IMS (78°C) t-Butanol (82°C)	2-Methoxyethanol **
Alcohols	1-Butanol (118°C) 2-Butanol (100°C)	1-Propanol (97°C) 2-Propanol (82°C) Methanol (65°C)	
Esters	t-Butyl acetate (95°C) Isopropyl acetate (89°C) Propyl acetate (102°C) Dimethyl Carbonate (91°C)	Ethyl acetate (77°C) Methyl acetate (57°C)	Methyl ethyl ketone
Ketones		Methyl isobutyl ketone (117°C) Acetone (56°C)	Benzene **
Aromatics		p-Xylene (138°C) Toluene ** (111°C)	Petroleum spirit ** 2-Methylpentane Hexane
Hydrocarbons		Isooctane (99°C) Cyclohexane (81°C) Heptane (98°C)	1,4-Dioxane ** 1,2-Dimethoxyethane ** Tetrahydrofuran Diethyl ether Diisopropyl ether **
Ethers		t-Butyl methyl ether (55°C) 2-Methyl THF (78°C) Cyclopentylmethyl ether (106°C)	Dimethyl formamide ** N-Methyl pyrrolidone ** N-Methyl formamide ** Dimethyl acetamide ** Acetonitrile
Dipolar aprotics		Dimethyl sulfoxide (189°C)	

\*\* = EHS Regulatory Alerts: please consult the detailed solvent guide and the GSK Chemicals Legislation Guide for more information <http://solventguide.gsk.com/>



**Figure 2.** GlaxoSmithKline (GSK) Solvent Selection Guide.

Figure reproduced from Henderson, R. K., et al, *Green Chemistry*, 2011, 13, 854–862 with permission of The Royal Society of Chemistry.

4. Henderson, R. K., et al., *Green Chemistry*, 2011, 13, 854–862.

## American Chemical Society Green Chemistry Institute Pharmaceutical Roundtable Solvent Selection Guide and Solvent Selection Tool

The American Chemical Society Green Chemistry Institute Pharmaceutical Roundtable (GCIPR) has collaboratively developed a solvent selection guide<sup>5</sup> for pharmaceutical companies. The guide rates solvents against 5 categories: safety, health, environment (air), environment (water), and environment (waste). Each category is scored between 1-10, with 10 being the highest concern.

The GCIPR also hosts an open access solvent selection tool<sup>6</sup> which is an approximate duplicate of the original tool built by AstraZeneca in Spotfire, a proprietary technology, that has been donated to the ACS GCIPR. More information about the tool can be found in the original work.<sup>7</sup> Check out the Beyond Benign webinar about this tool and more tools for innovation in chemistry from the ACS GCI Pharmaceutical Roundtable<sup>8</sup> and see Experiment 11 for an example of how these tools can be utilized in connection with this guide and in academic laboratory settings.

### *Additional Solvent Replacement Resources*

There are many other solvent substitution resources and guides within the pharmaceutical sector.<sup>9</sup> An excellent review and compilation of solvent selection guides by Prat *et. al.* has also been published in Green Chemistry.<sup>10</sup> The ACS GCIPR suggests the use of the CHEM21 solvent selection guide<sup>11</sup> which was developed to rate solvents based on health, safety, and environmental criteria. Additionally, this guide is aligned with the Global Harmonized System (GHS)<sup>12</sup> and European regulations. The CHEM21 solvent guide is geared toward academic partners and students, but still has some limitations.

- 
5. American Chemical Society Green Chemistry Institute Pharmaceutical Roundtable Solvent Selection Guide [<http://www.acs.org/content/acs/en/greenchemistry/industry-business/pharmaceutical.html>]
  6. American Chemical Society Green Chemistry Institute Pharmaceutical Roundtable Solvent Selection tool [<https://www.acs.org/content/acs/en/greenchemistry/research-innovation/tools-for-green-chemistry/solvent-tool.html>].
  7. Diorazio, L. J.; Hose, D. R. J.; Adlington, N. K., *Org. Process Res. Dev.* **2016**, *20*, 760–773.
  8. Beyond Benign, Tools for Innovation in Chemistry from the ACS GCI Pharmaceutical Roundtable Webinar [<https://www.beyondbenign.org/webinar/tools-for-innovation-in-chemistry-from-the-acsgci-pharmaceutical-roundtable/>].
  9. Prat, D., *et al.*, *Organic Process Research & Development*, **2013**, *17*, 1517–1525.
  10. Prat, D.; Hayler, J.; Wells, A., *Green Chemistry*, **2014**, *16*, 4546.
  11. D. Prat, *et al.*, CHEM21A solvent selection guide of classical- and less classical-solvents, *Green Chem.*, **2016**, *18*, 288–296.
  12. Globally Harmonized System of Classification and Labelling of Chemicals (GHS), seventh revised edition [[https://www.unece.org/trans/danger/publi/ghs/ghs\\_rev07/07files\\_e.html](https://www.unece.org/trans/danger/publi/ghs/ghs_rev07/07files_e.html)].

## CHEM21 selection guide of classical- and less classical-solvents

### *CHEM21 guide highlights*

#### Pros:

- Useful for quick selection of the greenest solvent by visual
- Survey comprised 53 classical solvents
- Encompasses newer solvents and bio-derived solvents
- A methodology that can give preliminary ranking of any solvent

#### Cons:

- Solvent ranking adapted to the pharmaceutical industry
- Boundaries between hazardous and highly hazardous cannot be clearly established due to not all companies listing the same banned solvents.
- Does not include supercritical fluids, gas expanding liquids, ionic liquids, high molecular weight glymes, fluorinated solvents, switchable solvents, deep eutectic solvents and Poly-Ethylene Glycols (PEGs).

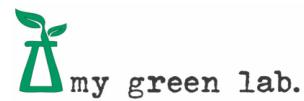
Recommended	Water, EtOH, i-PrOH, n-BuOH, EtOAc, i-PrOAc, n-BuOAc, anisole, sulfolane.
Recommended or problematic?	MeOH, t-BuOH, benzyl alcohol, ethylene glycol, acetone, MEK, MIBK, cyclohexanone, MeOAc, AcOH, Ac <sub>2</sub> O,
Problematic	Me-THF, heptane, Me-cyclohexane, toluene, xylenes, chlorobenzene, acetonitrile, DMPU, DMSO,
Problematic or hazardous?	MTBE, THF, cyclohexane, DCM, formic acid, pyridine.
Hazardous	Diisopropyl ether, 1,4-dioxane, DME, pentane, hexane, DMF, DMAc, NMP, methoxy-ethanol, TEA.
Highly hazardous	Diethyl ether, benzene, chloroform, CCl <sub>4</sub> , DCE, nitromethane, CS <sub>2</sub> , HMPA.

**Figure 3.** Figure adapted from the CHEM21 initial survey of publicly available solvent guides <sup>11, 13</sup>

The CHEM21 solvent selection guide<sup>11</sup> is one highlight of the CHEM21 Online Learning Platform<sup>13</sup> created as part of the IMI funded CHEM21 project, Chemical Manufacturing Methods for the 21<sup>st</sup> Century Pharmaceutical Industries, which aims to develop new reactions or methodologies with

---

13. CHEM21 Online Learning Platform [<http://learning.chem21.eu/>].



improved green metrics over existing tools to improve the sustainability of the syntheses of pharmaceutical products. The project has a strong emphasis on education and training both of existing and future generations of medicinal and process chemists. For more solvent rankings from CHEM21 visit the CHEM21 Online Learning Platform<sup>13</sup> or the CHEM21 A solvent selection guide of classical- and less classical-solvents publication.<sup>11</sup>

## Beyond Benign Solvent Guide Magnet

Beyond Benign has created a Greener Solvent Guide magnet for commonly used solvents in teaching laboratories based off the solvent selection guides<sup>3,11,14,15</sup> and greener solvent alternatives available from Sigma-Aldrich.<sup>16</sup> The Greener Solvent Guide magnet uses the phrases and “traffic light” system of the CHEM21 solvent guide,<sup>11</sup> for a quick visual aid for selection of solvents with a lower safety, occupational health, environmental, cost and industrial constraints. The Greener Solvent Guide also utilized the Pfizer solvent replacement table approach,<sup>3</sup> which can be used to guide “greener” choices for solvents. The magnet also contains resources highlighted in this guide. [Contact Beyond Benign](#) to receive a magnet for your teaching laboratory, office and/or research laboratory.

### Greener Solvent Guide

For more resources for Green Chemistry in chemistry education:  
<http://bit.ly/gc-resources>

Key:	Hazardous	Problematic	Preferred
* Indicates Highly Hazardous			

Undesirable Solvents	Alternative
<b>Pentane, Hexane(s)</b>	<b>Heptane</b>
<b>DMF, DMAc, NMP, DMSO</b>	<b>Acetonitrile, Cyrene<sup>c</sup>, Cyclopentyl methyl ether (CPME)<sup>a</sup>, dimethyl carbonate<sup>c</sup></b>
<b>Tetrahydrofuran, Methyl tert-butyl ether (MTBE)</b>	<b>2-Methyltetrahydrofuran (2-MeTHF), CPME</b>
<b>Di-isopropyl ether or diethyl ether*</b>	<b>2-MeTHF or tert-butyl methyl ether, CPME</b>
<b>Dioxane or dimethoxyethane</b>	<b>2-MeTHF or tert-butyl methyl ether, CPME</b>
<b>Chloroform*, dichloroethane* or CCl<sub>4</sub>*</b>	<b>Dichloromethane</b>
<b>Pyridine (as a base)</b>	<b>Triethylamine (Et<sub>3</sub>N)</b>
<b>Dichloromethane (in extractions)</b>	<b>Ethyl acetate (EtOAc), MTBE, toluene, 2-MeTHF</b>
<b>Dichloromethane (in chromatography)</b>	<b>EtOAc/heptane<sup>b</sup>, 3:1 EtOAc/EtOH<sup>b</sup></b>
<b>Benzene*</b>	<b>Toluene</b>
<b>Acetone</b>	<b>Ethyl lactate<sup>a</sup></b>

For a review of organic reactions in water: <http://bit.ly/org-rx-water>

For a review of solvent-free organic reactions: <http://bit.ly/solvent-free-org-rx>

#### References:

a. Prat, D., et al., *Green Chemistry*, **2016**, *18*, 288–296; Dunn, P. J., et al., *Green Chemistry*, **2008**, *10*, 31–36.

a. MilliporeSigma Greener Solvent Alternatives [<https://www.sigmaaldrich.com/technical-documents/articles/analytical/solvents-and-reagents/greener-solvent-alternatives.html>].

b. Taygerly, J.P., et al., *Green Chemistry*, **2012**, *14*, 3020–3025.

c. Byrne, F.P., et al., *Sustain Chem Process*, **2016** *4*; 7 1–24.

V.1 March 2020

**Figure 4.** The Beyond Benign Greener Solvent Guide of classically used solvents for teaching laboratories based off the solvent selection guides and greener solvent alternatives available from Sigma-Aldrich.

- 
- 14. Taygerly, J.P.; Peterson, E. A., et al., *Green Chemistry*, **2012**, *14*, 3020–3025.
  - 15. Byrne, F.P., et al., *Sustain Chem Process*, **2016** *4*; 7 1–24.
  - 16. MilliporeSigma Greener Solvent Alternatives [<https://www.sigmaaldrich.com/technical-documents/articles/analytical/solvents-and-reagents/greener-solvent-alternatives.html>].

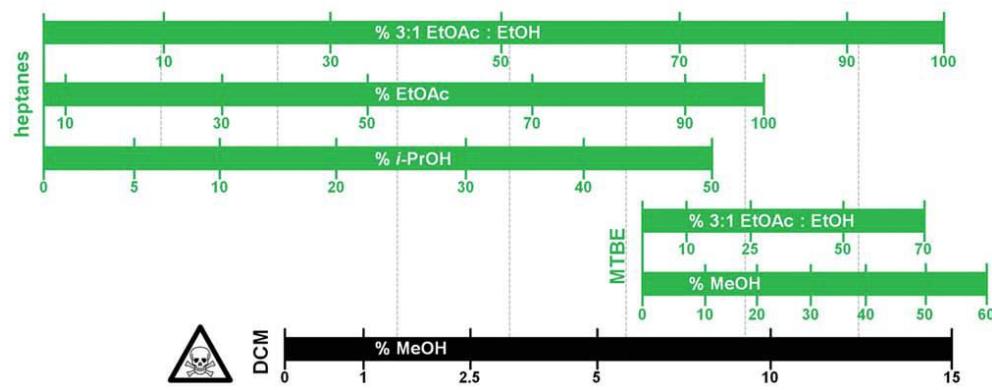
## Alternatives to Dichloromethane in Chromatography

“A convenient guide to help select replacement solvents for dichloromethane in chromatography”<sup>14</sup>

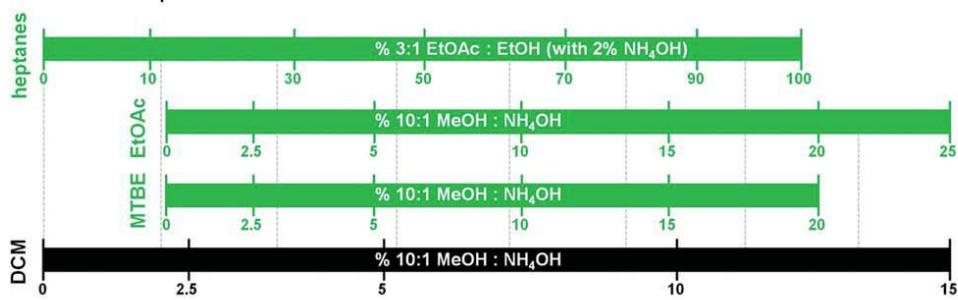
A 3:1 (v/v) solution of ethyl acetate/ethanol has been found to a viable alternative for dichloromethane (DCM) in flash chromatography and HPLC. This alternative is based on a publication in the journal *Green Chemistry* by Taygerly and Peterson titled “A convenient guide to help select replacement solvents for dichloromethane in chromatography”.<sup>14</sup> The chromatography guide is experimentally-derived, and provides chemists options for choosing greener options, with a particular focus on the use of DCM. The guide itself was developed for use by medicinal chemists looking for alternatives to DCM and methanol, which is widely used by chemists to purify their compounds. The quick-reference guide (Figure 5) provides chemists with a reference tool for guiding the substitution according to solvent polarity and eluting ability. The tool cross-references these properties to guide users towards the following greener options for solvents: heptanes, ethyl acetate: ethanol, isopropanol, and methyl t-butyl ether. Sigma-Aldrich offers a greener alternative to chlorinated solvents (in particular, DCM) in chromatography, ethyl acetate/ethanol 3:1 (v/v) solution ([Sigma-Aldrich SKU 745588](#)).

## Relative Eluting Strengths of Green Chromatography Solvent Mixtures

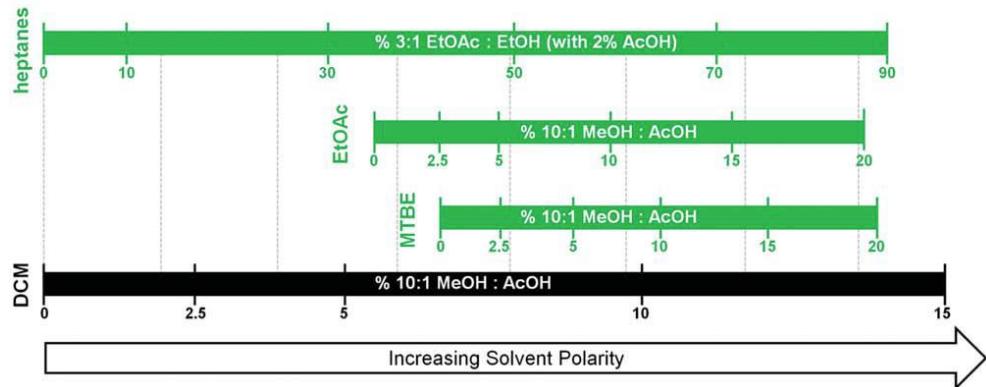
### Neutral Compounds



### Basic Compounds



### Acidic Compounds



**Figure 5.** Green Chromatography Solvent Selection Guide. Starting from the appropriate DCM–MeOH concentration, compare vertically across the bar chart to identify greener solvent mixtures of similar eluting ability. For example, if a compound suitably elutes in 5% DCM–MeOH in the absence of an additive, the “Neutral Compounds” bar chart predicts that 60% 3:1 EtOAc : EtOH in heptanes or 40% *i*-PrOH in heptanes would be suitable starting points to evaluate greener solvent alternatives. Figure reproduced from Taygerly, J.P.; Peterson, E. A., *et al.*, *Green Chemistry*, 2012, 14, 3020–3025 with permission of The Royal Society of Chemistry.

### Biorenewable Dipolar Aprotic Alternative – Cyrene™

Cyrene™ [(-)-Dihydrolevoglucosenone] is a safer, biorenewable alternative to petroleum-derived dipolar aprotic solvents such as, dimethylformamide (DMF) and n-methyl-2-pyrrolidone (NMP).<sup>17, 18</sup> The latter two chemicals were recently added to the European Chemical Agency's (ECHA) candidate list of Substances of Very High Concern (SVHC) for Authorisation. Cyrene™ was developed by Circa Group in partnership with Professor James Clark, Ph.D., at the University of York's Green Chemistry Centre of Excellence (GCCE) in 2014 and only recently has become available for purchase in the quantities required for solvent usage. Despite the supply limitations initially, Cyrene™ has been successfully utilized as a greener substitute in industrially relevant applications by researchers in graphene synthesis,<sup>19</sup> carbon cross-coupling reactions<sup>20</sup> and in the synthesis of metal-organic frameworks.<sup>21</sup> Cyrene™ is now commercially available ([Sigma-Aldrich SKU 807796](#)) at quantities required for solvent usage and can replace solvents such as dimethylformamide (DMF), dimethylacetamide (DMAc), n-methyl-2-pyrrolidone (NMP) and dimethyl sulfoxide (DMSO) as a safer and biorenewable alternative. Learn more about greener alternatives solvents commercially available from MilliporeSigma [here](#).

### Solvent Substitution – no universal approach

Solvent selection guides are methodologies and visual aids which rank solvents, many companies and institutions have complied guides. These guides can help chemist find solvents with low toxicity, minimal safety concerns and little environmental impact. *Remember there is no universal approach to solvent selection.* Solvent guides are resources that should be used by chemist to make the right choice for their specific chemistry. The next time you step into the lab consider what you have learned here and deliberate if you are using the ideal solvent to give your reaction the best overall sustainability profile possible.

---

17. CYRENE™: A New Bio-based Dipolar Aprotic Solvent

[<https://communities.acs.org/community/science/sustainability/green-chemistry-nexus-blog/blog/2018/02/21/cyrene-a-new-bio-based-dipolar-aprotic-solvent>].

18. The Future of Solvents Bio Renewable [[https://www.sigmaaldrich.com/content/dam/sigma-aldrich/docs/Sigma-Aldrich/General\\_Information/1/greener-solvents-br-ms.PDF](https://www.sigmaaldrich.com/content/dam/sigma-aldrich/docs/Sigma-Aldrich/General_Information/1/greener-solvents-br-ms.PDF)].

19. Salavagione, H. J., et al., *Green Chem.* **2017**, *19*, 2550–2560.

20. a) Wilson, K. L., et al., *Beilstein J. Org. Chem.* **2016**, *12*, 2005–2011; b) Wilson, K. L., et al., *Synlett*, **2017**, *28*, A–E.

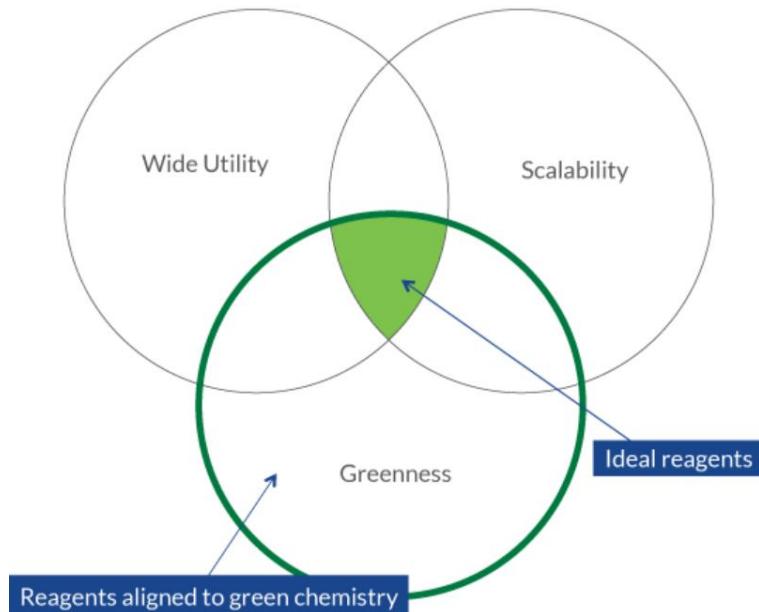
21. Zhang, J., et al., *ACS Sustainable Chem. Eng.*, **2016**, *2*, 7186–7192.

## Reagent Selection Guides

Reagent selection guides function similarly to solvent selection guides, by assisting users to select the greenest reagent for a particular chemical transformation by combining health, safety, and environmental considerations.

## ACS GCI Reagent Guides

The ACS GCI Pharmaceutical Roundtable has developed an online tool to guide chemists towards the greener selection of reagents in chemical transformations.<sup>22</sup> The tool presents the user with a Venn diagram representing three factors for the selection of reagents: wide utility, scalability, and greenness.



**Figure 6.** ACS GCI Pharmaceutical Roundtable Reagent Guide Venn diagram.

The ideal reagent is centrally located at the intersection of all three circles. Each reagent within the Venn diagrams are hyperlinked to further information and lists the primary references. Placements within the Venn can change with many variables (solvent, catalyst, treatment of wastes etc.). As outlined, these diagrams can give a good estimate for greener reagents and discussion of the greenest reagent under specific conditions is actively encouraged. To learn

22. ACS GCI Pharmaceutical Reagent Guides [<https://reagents.acsgcipr.org/>].

more about this tool and more tools for innovation in chemistry from the ACS GCI Pharmaceutical Roundtable check out the Beyond Benign webinar archive.<sup>23</sup>

### GlaxoSmithKline (GSK) Reagent Guides

With the aim to reduce the environmental impacts of drug discovery and development GSK developed reagent guides ranking commonly used reagent for 15 chemical transformations. The GSK guides cover alkene reduction, amide formation, C–H bromination, C–H chlorination, deoxychlorination, epoxidation, ester formation, ether formation, fluorination, iodination, ketone reduction, nitro reduction, oxidation of alcohols to aldehydes and ketones, reductive amination and sulfur oxidation.<sup>24</sup> Using the same assessments and calculations performed for the aforementioned transformations GSK created acid and base guides, although not all acids and bases are interchangeable the guides help encourage sustainability when planning chemical transformations.<sup>25</sup> Notably, recently the GSK guides have been used to develop Green Chemistry assignments<sup>26</sup> and case studies can be found on the CHEM21 Online Learning Platform.<sup>13</sup>

---

23. Beyond Benign, Tools for Innovation in Chemistry from the ACS GCI Pharmaceutical Roundtable Webinar [<https://www.beyondbenign.org/webinar/tools-for-innovation-in-chemistry-from-the-acsgci-pharmaceutical-roundtable/>]

24. Adams, J. P., et al., *Green Chem.*, **2013**, *15*, 1542–1549.

25. Henderson, R. K., et al., *Green Chem.*, **2015**, *17*, 945–949.

26. Obhi, N. K., et al., *J. Chem. Educ.*, **2019**, *96*, 93–99.

## Greener Laboratory Techniques

### A Brief Overview of Greener Recommendations to Common Synthetic Techniques

#### Distillation: Simple and Fractional

Simple and fractional distillations are common techniques in the general and organic chemistry teaching laboratory, most notably for use in purifications and in boiling point determination. Organic solvents such as toluene and cyclohexane are commonly used to demonstrate the separation of solvent mixtures through distillation.<sup>27</sup> Ethanol-water mixtures can also be used, and the purified ethanol tested for purity through an ignition test.<sup>28</sup>

Laboratory experiments demonstrating acetone recovery are also being performed as means for teaching students the importance and potential of solvent recycling.<sup>29</sup> The table below lists commonly used distillation solvents and their relative solvent ranking back on the solvent selection guides.

**Table 2.** Commonly used distillation solvents and their relative solvent ranking.

Chemical Name Sigma-Aldrich Catalog #	Solvent ranking based on solvent selection guides <sup>11</sup>
Cyclohexane 227048	Problematic or Hazardous
Toluene 244511	Problematic
Acetone 650501	Recommended or Problematic
Ethanol 459836	Recommended
Water 99053	Recommended

The isolation of natural products by distillation is one of the hallmark practices in organic chemistry. The steam distillation of (+)-limonene from orange peels<sup>30</sup>, eugenol, anethole, and

27. Simple and Fractional Distillation of a Cyclohexane-Toluene Mixture, Macroscale and Microscale Organic Exp., Williamson, K. L., Masters, K. M., 6th Ed, Brooks/Cole Cengage Learning, 2011, pp. 92–95.

28. Simple Distillation of an Ethanol-Water Mixture, Macroscale and Microscale Organic Experiments, Williamson, K. L., Masters, K. M., 6th Edition, Brooks/Cole Cengage Learning, 2011, pp. 93–95.

29. Weires, N. A., Recycling of Waste Acetone by Fractional Distillation *et al.*, *J. Chem. Educ.*, **2011**, *88*, 1724–1726.

30. a) Greenberg, F. H., Natural Products Isolation – Orange Oil: An Undergraduate Organic Experiment. *J. Chem. Educ.* **1968**, *45*, 537; b) Garner, C. M.; Garibaldi, C., A Microscale Isolation of Limonene from Orange Peels. *J. Chem. Educ.* **1994**, *71*, A146.

carvone from spices<sup>31</sup> and thymol from thyme, citral from lemongrass, or camphor from sagebrush are some examples from the literature.<sup>32</sup> An alternative method to traditional steam distillation has also been explored and published.<sup>33</sup>

### Chromatography: TLC and Column

Chromatography techniques are essential in the organic chemistry laboratory for identifying whether the desired reaction has occurred, if starting materials are present, for testing the purity of a product, and product purification. The choice of chromatography solvent can be limited due to the required solvent properties for the eluting solvent. There are many available resources for guiding chemists towards greener solvent choices, the majority of which were outlined in the above introduction section *Solvent Selection Resources*. Simple solvent substitutions can have considerable impact, especially minimizing the use of chlorinated solvents.<sup>3,14</sup>

The table below lists commonly used solvents in chromatography and their relative EH&S information. Please refer to the solvent selection resources in the introduction of this resource for further information regarding solvent substitution.

**Table 3.** Commonly used solvents in chromatography and their relative solvent ranking.

Chemical Name Sigma-Aldrich Catalog #	Solvent ranking based on solvent selection guides <sup>11</sup>
Hexane 296090	Hazardous
Heptane 246654	Problematic
Dichloromethane 676853	Problematic or hazardous
Ethyl acetate 270989	Recommended

31. O’Shea, S. K., et. al., Isolation and Analysis of Essential Oils from Spices. *J. Chem. Educ.* **2012**, 89, 665–668.

32. McLain, K. A., et. al., Introducing Organic Chemistry Students to Natural Product Isolation Using Steam Distillation and Liquid Phase Extraction of Thymol, Camphor, and Citral, Monoterpenes Sharing a Unified Biosynthetic Precursor. *J. Chem. Educ.* **2015**, 92, 1226–1228.

33. Just, J., et. al., Extraction of Eugenol from Cloves Using an Unmodified Household Espresso Machine: An Alternative to Traditional Steam-Distillation. *J. Chem. Educ.* **2016**, 93, 213–216.

Greener chromatography experiments often involve the separation of pigments from plants and include the use of recycled solvents in the extraction process<sup>34</sup> and microcolumn chromatography.<sup>35</sup> The utilization of alternative media within column chromatography is another greener approach.<sup>36</sup>

### Extraction

Extraction techniques are commonly performed as a means for isolating and purifying a product (i.e., essential oil or natural product extraction). Solvents commonly used in extractions include methylene chloride, petroleum ether, or hexanes. Greener solvent choices can be explored for solvents that have similar properties (e.g. miscibility, boiling point), and can often seamlessly replace traditional solvents.

The table below lists commonly used solvents for extractions and their relative solvent ranking based on the CHEM 21 overall ranking of solvents guide.<sup>11</sup> Refer to the Solvent Selection Resources in the introduction of this resource for further information regarding solvent substitution.

**Table 4.** Commonly used solvents for extractions and their relative solvent ranking

Chemical Name Sigma-Aldrich Catalog #	Solvent ranking based on solvent selection guides <sup>11</sup>
Dichloromethane 676853	Problematic or hazardous
Petroleum ether 320447	Hazardous
Hexane 296090	Hazardous
Heptane 246654	Problematic
Ethyl acetate 270989	Recommended
Isopropanol 278475	Recommended

34. McDougal, O.M., et. al., A Green Approach To Separate Spinach Pigments by Column Chromatography, *J. Chem. Educ.*, **2013**, *90*, 796–798.

35. Ciaccio, J. A., et. al., Modified Method for Extraction of Photosynthetic Plant Pigments for Microcolumn Chromatography. *J. Chem. Educ.* **2020**, *97*, 2362–2365.

36. Dias, A. M., La Salete Ferreira, M. Supermarket Column Chromatography of Leaf Pigments Revisited: Simple and Ecofriendly Separation of Plant Carotenoids, Chlorophylls, and Flavonoids from Green and Red Leaves. *J. Chem. Educ.* **2015**, *92*, 189–192.

A greener extraction procedure for use within the organic chemistry laboratory involves the extraction of avocado oil using ethyl acetate and isopropanol. The oil is then used in the making of an avocado soap.<sup>37</sup> Microscale approaches can reduce solvent waste<sup>38</sup> and the antibacterial properties of extracted natural products can highlight toxicology principles.<sup>39</sup> Both liquid and supercritical carbon dioxide have been used as substitutes for organic solvents in extraction and chromatographic methods.<sup>40</sup> Carbon dioxide is advantageous because it can be obtained from and returned to the environment and is neither toxic nor flammable which increases the safety of extraction procedures.

- 
37. Sutheimer, S., et. al., Green Soap: An Extraction and Saponification of Avocado Oil. *J. Chem. Educ.*, **2015**, *92*, 1763–1765.
38. Na Ayudhya, T. I., Using a Microscale Approach To Rapidly Separate and Characterize Three Photosynthetic Pigment Species from Fern. *J. Chem. Educ.* **2015**, *92*, 920–923.
39. Purcell, S. C., et. al., Extraction and Antibacterial Properties of Thyme Leaf Extracts: Authentic Practice of Green Chemistry. *J. Chem. Educ.* **2016**, *93*, 1422–1427.
40. a) McKenzie, L. C., et. al., Green Chemical Processing in the Teaching Laboratory: A Convenient Liquid CO<sub>2</sub> Extraction of Natural Products. *Green Chem.* **2004**, *6*, 355–358; b) Schaber, P. M., et. al., Supercritical Fluid Extraction Versus Traditional Solvent Extraction of Caffeine From Tea Leaves: A Laboratory-Based Case Study for an Organic Chemistry Course. *J. Chem. Educ.* **2012**, *89*, 1327–1330; c) Buckley, H. L., et. al., Fitting It All In: Adapting a Green Chemistry Extraction Experiment for Inclusion in an Undergraduate Analytical Laboratory. *J. Chem. Educ.* **2013**, *90*, 771–774; d) Bodsgard, B. R., et. al., Liquid CO<sub>2</sub> Extraction and NMR Characterization of Anethole From Fennel Seed: A General Chemistry Laboratory. *J. Chem. Educ.* **2016**, *93*, 397–400; e) Baldwin, B. W., et. al., Liquid CO<sub>2</sub> in Centrifuge Tubes: Separation of Chamazulene From Blue Tansy (*Tanacetum Annum*) Oil via Extraction and Thin-Layer Chromatography. *J. Chem. Educ.* **2018**, *95*, 620–624; f) Baldwin, B. W., et. al., Extraction of dyes contained in glow sticks using liquid CO<sub>2</sub>. *Green Chemistry Letters and Reviews* **2019**, *12*, 102–106.

## Reaction Selection Resources for Organic Chemistry Laboratories

Greener alternatives to organic chemistry reactions have been on the rise since the early 2000's, when new publications began to appear that presented easily adoptable options for greener organic chemistry experiments.

Key publications and websites for greener alternative organic laboratory exercises include:

1. Doxsee, K., Hutchison, J. *Green Organic Chemistry: Strategies, Tools, and Laboratory Experiments*, Brooks/Cole, Pacific Grove, CA, 2004.
2. Kirchhoff, M., Ryan, M.A., Eds., *Greener Approaches to Undergraduate Chemistry Experiments*, American Chemical Society, Washington, DC, 2002.
3. Roesky, H., Kennepohl, D., Eds., *Experiments in Green and Sustainable Chemistry*, Wiley-VCH, Weinheim, 2009.
4. Dicks, A. P., Ed., *Green Organic Chemistry in Lecture and Laboratory*, CRC Press Taylor & Francis Group, Boca Raton, FL, 2012.
  - This publication includes an appendix of greener organic chemistry reactions. The appendix profiles 178 reactions covering the typical reactions taught within the organic laboratory course, and includes the primary literature reference, experimental technique employed, and greener principles highlighted.
5. Mohan, R. S.; Mejia, M. P., Environmentally Friendly Organic Chemistry Laboratory Experiments for the Undergraduate Curriculum: A Literature Survey and Assessment. *J. Chem. Educ.* **2020**, 97, 943–959.
6. a) Leontyev, A., et al., OrganicERs: Building a Community of Practice for Organic Chemistry Instructors through Workshops and Web-Based Resources. *J. Chem. Educ.* **2020**, 97, 106–111; b) Organic Education Resources (OrganicERs) [<https://www.organicers.org/>].

## Organic Reactions under Aqueous or Solvent-Free Conditions

### *Aqueous Organic Reactions*

Inspired by nature's use of water as the universal solvent and its low cost, abundance, low toxicology, and lack of flammability chemists have been exploring organic reactions in water. Recently, Lipshutz and co-workers have created several surfactants to facilitate organic transformations under aqueous conditions. These surfactants naturally form micelles and micellar catalysis provides a pathway for synthesizing novel and conventional materials in aqueous media. In partnership with the Lipshutz research group, MilliporeSigma has made these surfactants commercially available ([Sigma-Aldrich SKU 698717, 763896 and 776033](#)) and kits for ten water-friendly transition metal-catalyzed cross-coupling reactions are available for purchase through Sigma-Aldrich ([Sigma-Aldrich SKU 802271, 802298, 802301, 802328, 802336, 802344, 802352, 802360, 802379, 802387](#)). Green Chemistry Principles 1 (waste prevention), 5 (safer solvents and auxiliaries), 6 (design for energy efficiency) and 9 (catalysis) can be employed when

using micellar catalysis. Learn more from Professor Lipshutz about how the Future of Organic Synthesis is in Water: From Chemo-to Biocatalysis in the American Chemical Society webinar.<sup>41</sup>

Key publication for greener alternative organic laboratory exercises include:

1. Dicks, A. P. A Review of Aqueous Organic Reactions for Undergraduate Teaching Laboratory. *Green Chemistry Letters and Reviews*. **2009**, 2, 9–21, and references therein.
2. Lipshutz, B. H., *et al.*, “Click” and Olefin Metathesis Chemistry in Water at Room Temperature Enabled by Biodegradable Micelles. *J. Chem. Educ.* **2013**, *90*, 1514–1517.
3. Landstrom, E. B., *et al.*, Discovery-Based S<sub>N</sub>Ar Experiment in Water Using Micellar Catalysis. *J. Chem. Educ.* **2019**, *96*, 2668–2671.
4. Shimizu, E. A., *et al.*, Aqueous Dearomatization/Diels-Alder Cascade to a Grandifloracin Precursor. *J. Chem. Educ.* **2019**, *96*, 998–1001.

### *Solvent-Free Organic Reactions*

Solvents are used in large volumes in reactions and in purification techniques traditionally in the laboratory settings. However, solvents do not determine the composition of the product, nor are they active components of a formulation, so are they really needed? Organic reactivity in the absence of solvent has been explored for the past 20 years due to the advantages of eliminating waste (Principle 1) and designing for energy efficiency (Principle 6) along with faster reactions under conditions such as grinding, microwave, irradiation, or mechanical stirring in the presence or absence of heat when compared to traditional approaches. Exposing students to solvent-free reactions can break their false impressions that solvents are an essential part of the design process for any organic transformation and highlight Green Chemistry Principles.

Key publication for greener alternative organic laboratory exercises include:

1. Dicks, A. P. Solvent-Free Reactivity in the Undergraduate Organic Laboratory. *Green Chemistry Letters and Reviews*. **2009**, 2, 87–100.
2. Patterson, A. L., *et al.*, Solvent-Free Synthesis and Fluorescence of a Thiol-Reactive Sensor for Undergraduate Organic Laboratories. *J. Chem. Educ.* **2013**, *90*, 1685–1687.
3. Colacino, E., *et al.*, Introducing Students to Mechanochemistry via Environmentally Friendly Organic Synthesis Using a Solvent-Free Mechanochemical Preparation of the Antidiabetic Drug Tolbutamide. *J. Chem. Educ.* **2019**, *96*, 766–771.
4. Omar, Y. M., *et al.*, Solvent-Free N-Formylation: An Experimental Application of Basic Concepts and Techniques of Organic Chemistry. *J. Chem. Educ.* **2020**, *97*, 1134–1138.
5. Touaibia, M., *et al.*, Green Hydrogenation: Solvent-Free Hydrogenation of Pinenes for an Undergraduate Organic Chemistry Laboratory. *J. Chem. Educ.* **2020**, *97*, 2296–2301.

---

41. The Future of Organic Synthesis is in Water: From Chemo- to Bio-catalysis  
[\[https://www.acs.org/content/acs/en/acs-webinars/technology-innovation/water-chemistry.html\]](https://www.acs.org/content/acs/en/acs-webinars/technology-innovation/water-chemistry.html).

## Incorporating Research into the Organic Laboratory Curriculum

Research-integrated laboratories are now understood to be more effective than teaching student through the traditional expository experimental approaches, however the activation barrier to this change is high. Many publications explain methods for incorporating research into the undergraduate curriculum.

Key publications and resources to lower the barrier to integrating research into the laboratory curriculum:

1. a) Lee, N. E., *et al.*, Using Green Chemistry Principles As a Framework To Incorporate Research into the Organic Laboratory Curriculum. *J. Chem. Educ.* **2014**, *91*, 1001–1008, and references therein; b) Gurney, R. [Using Green Chemistry Principles As a Framework To Incorporate Research into the Organic Laboratory Curriculum Webinar](#).
2. Gurney, R. and Lee, N. E. [A Practical Guide to Introducing Research Integration into a Chemistry Lab Curriculum](#).
3. Wu, N., *et al.*, Student-Designed Green Chemistry Experiment for a Large-Enrollment, Introductory Laboratory Course. *J. Chem. Educ.* **2019**, *96*, 2420–2425.
4. Josephson, P., *et al.*, Student-Driven Development of Greener Chemistry in Undergraduate Teaching: Synthesis of Lidocaine Revisited. *J. Chem. Educ.* **2019**, *96*, 1389–1394.
5. Cruz, C. L., *et al.*, Development of a Large-Enrollment Course-Based Research Experience in an Undergraduate Organic Chemistry Laboratory: Structure-Function Relationship in Pyrylium Photoredox Catalysts. *J. Chem. Educ.* **2020**, *97*, 1572–1578.



## Reactions Selected for Assessment

Select resources have been identified within this guide to facilitate the adoption of greener alternatives to experiments traditionally conducted within the undergraduate organic chemistry laboratory curriculum. This guide contains the following reactions:

Experiment 1: Aldol Condensation

Experiment 2: Esterification

Experiment 3: Oxidation

Experiment 4: Diels-Alder

\*Experiment 5: Electrophilic Aromatic Substitution

Experiment 6: Substitution ( $S_N2$ )

\*Experiment 7: Bromination

\*Experiment 8: Reduction

Experiment 9: Friedel-Crafts Alkylation and Acylation

Experiment 10: Polymerization

Experiment 11: Wittig

Experiment 12: Grignard

*\*New experiments added since 2018 version of this resource guide.*

## Methodology used for Quantitative and Qualitative Assessment for this Guide

Each reaction has been measured by quantitative and qualitative means. The quantitative assessment includes a volume of waste estimate, and an environmental, health and safety assessment. The qualitative assessment includes the flagging of the reaction for the following green chemistry principles: use of renewable feedstocks, energy efficiency, catalysis, safer solvents and auxiliaries, and accident prevention. Each estimate includes assumptions and are based on widely available data-sets and/or resources, which are outlined further below.

### *Qualitative Assessment*

Chemicals and chemical reactions are flagged for the following qualitative benefits: less hazardous chemical synthesis, use of renewable feedstocks, energy efficiency, catalysis, safer solvents and auxiliaries, and accident prevention. Each qualitative endpoint is described further:

Qualitative Endpoint	Icon	Criteria
Less Hazardous Chemical Synthesis		Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
Renewable Feedstocks		The chemical can be derived from a renewable feedstock. For example: ethanol can be derived from bio-based feedstocks
Energy Efficiency		The reaction uses comparatively less energy than the traditional reaction procedure. For example: the grinding of two reagents at room temperature using a mortar and pestle versus heating to reflux.
Catalysis		The use of catalytic reagents as opposed to stoichiometric reagents.
Safer Solvents and Auxiliaries		The use of safer solvents as compared to traditional alternatives (see Safer Solvent section).
Accident Prevention		The avoidance of the use of substances that have potential for chemical accidents, including releases, explosions and fires. For example: avoiding the use of a pyrophoric reagent

### Volume of Waste Estimate

This analysis assumes that all solvents, reagents and products will be transformed to waste products. We understand that some products will be used as starting materials for a subsequent reaction. However, in our assessment, we are assuming that the product will be minimal in relation to the waste created and that the products are eventually discarded as waste. We have made note of where aqueous waste is created that can be neutralized before disposal, which may decrease the amount of liquid waste disposed.

### Green Chemistry Metric: DOZN™ 2.0

We all want to make greener choices but how can we be sure it is a greener choice? Metrics! [Milliporesigma](#) has created a Quantitative Green Chemistry Evaluator, simply referred to as DOZN™ 2.0 as it enables consistent evaluation of different products and processes against the 12 Principles of Green Chemistry. The quantitative approach allows for clarifying what is “greener” about a greener product or process. To evaluate the products and processes using DOZN™ 2.0, the 12 Principles of Green Chemistry into three major groups: improved resource use, increased energy efficiency, and reduced human and environmental hazards. Below is a table which shows the grouping of the Principles. An aggregate score is then calculated on a scale of 0-100, 0 being the most desired.

Improved Resource Use	Increased Energy Efficiency	Reduced Human and Environmental Hazards
Principle 1: Waste prevention	Principle 6: Design for energy efficiency	Principle 3: Less hazardous chemical synthesis
Principle 2: Atom economy		Principle 4: Designing safer chemicals
Principle 7: Use of renewable feedstock		Principle 5: Safer solvents and auxiliaries
Principle 8: Reduce derivatives		Principle 10: Design for degradation
Principle 9: Catalysis		Principle 12: Inherently safer chemistry for accident prevention
Principle 11: Real-time analysis for pollution prevention		

Why did MilliporeSigma create this tool? To show customers the value and improvements made to their re-engineered products. Products in the re-engineered category have been manufactured by scientists directed by members of the Worldwide Green Chemistry Committee who have developed new ways to manufacture the products that use fewer resources, are less hazardous and/or generate less waste. The DOZN™ 2.0 scoring system quantifies the improvement in the environmental footprint of the re-engineered product.

To see what products have been re-engineered by MilliporeSigma visit their [greener alternatives website](#). One example is the re-engineering of β-Amylase, a simple comparison of the processes can be observed in Figure 7.

β-Amylase—an enzyme commonly found in sweet potatoes—hydrolyzes starch into sugar.



**6,000 lbs**

of sweet potatoes



**1,900 gallons**

of acetone



**2,000 lbs**

of sweet potatoes



**No solvent required**



**Significant use**

of electricity



**Minimal electricity use**

**Figure 7.** Impacts of re-engineering β-Amylase process.

The full comparison of the DOZN™ 2.0 scoring and the improvements made can be seen [here](#).

### *Academic Use of DOZN™ 2.0*

DOZN™ 2.0 simplifies the analysis of Green Chemistry because it provides a quantification of each of the twelve principles by yielding a positive number for each principle. Giving students a tangible entity, like a number, will make Green Chemistry seem more approachable by decreasing the amount of qualification-based analysis required by the students. Also, by quantifying each of the twelve principles, students will be able to determine the percent improvement of each principle which would not be possible if only qualification-based analysis methods were used. Another advantage of DOZN™ 2.0 is that it will teach students about chemical safety and also overall sustainability while in the lab. By enlightening students about potential chemical hazards, students will be more mindful of their own safety. In addition, the environmental effects the chemicals have will help emphasize why they should only obtain the correct amount of chemicals and why they should always properly dispose of their chemical waste.

DOZN™ 2.0 can also help chemical educators and researchers who wish to design or modify laboratory experiments. For example, if a researcher wanted to replace hazardous solvent after reviewing the solvent selection guides highlighted within the guide , they could first enter both procedures into DOZN 2.0 to see how the overall greenness of the procedure would change and possibly help them justify the change on the basis of the human and environmental impacts.

### *Connection to Safety*

RAMP an acronym standing for Recognize hazards, Asess the risks of the hazard, Minimize the risk of the hazard and Prepare for emergencies is an easy to remember approach to chemical safety. The RAMP framework and Green Chemistry are complementary to each other and the use of Green Chemistry metrics, such as DOZN™ 2.0, explored further here is an example of recognizing (R) and assessing (A) the risks of hazards in chemical reactions. With the Green Chemistry framework, minimizing (M) the risks can be achieved by elimination or substitution of hazardous substances and many resources are available to provide alternatives. Therefore, training on the theory and application of Green Chemistry Principles results in protecting and improving the safety of those working in the chemistry laboratory. Utilizing DOZN™ 2.0 in an academic laboratory setting will allow students an introduction to Green Chemistry and the twelve principles of Green Chemistry in simplified terms.

To use DOZN™ 2.0, a bio-hazard score (B score) of each material in the chemical reaction is needed and can teach safety through recognizing and assessing the risks associated with each chemical. The B score is gathered from the Globally Harmonized System (GHS) environmental hazard criteria of the raw material (chemical) and any of its degradation products (if readily degradable). In order to calculate the B score, the Safety Data Sheet (SDS) of the raw material (chemical) is needed, exposing students to using SDS data.

To determine the B score for a chemical the following SDS sections are used to gather data:

- GHS Classification (section 2.1) for aquatic toxicity
- Hazardous decomposition product(s) (section 10.6)
- Ecological information (section 12) for data on acute aquatic toxicity or chronic aquatic toxicity (NOEC (fish daphnia)) for product(s) that readily degrade

The B score of the raw material is the highest of the decomposition product(s). For example, if a product has a GHS score of 4 in all present categories then its B score is 1. However, if it has a GHS score of 4 for acute aquatic toxicity and 2 for chronic aquatic toxicity then the B score for the raw material is 3.

B Score and GHS Relationship				
Element <sup>42</sup>	GHS Category 1	GHC Category 2	GHS Category 3	GHS Category 4
<b>Acute aquatic Toxicity</b>	≤1.00 mg/L	> 1.00 but ≤ 10.0 mg/L	> 10.00 but ≤ 100.0 mg/L	> 100 mg/L
<b>Chronic aquatic toxicity, NOEC (fish, daphnia)</b>	≤1.00 mg/L	> 1.00 but ≤ 10.0 mg/L	> 10.00 but ≤ 100.0 mg/L	> 100 mg/L
<b>B Score</b>	<b>4</b>	<b>3</b>	<b>2</b>	<b>1</b>

Finding the GHS classification information from the SDS is a fundamental way of assessing the risk of a chemical and teaches students to apply this information rather than just comply with a chemical assessment alone. Overall, incorporating DOZN™ 2.0 into an academic teaching laboratory can add another layer to the student's scientific experiences by allowing them to think beyond the mere act of performing the experiment. By educating students about the 12 Principles of Green Chemistry through DOZN™ 2.0, students can be inspired and motivated to seek further education or careers in such an emerging field as Green Chemistry.

#### *Does No Data mean Safe?*

What does it mean when there are no H phrases on an SDS? Does that mean a chemical is safe? Not necessarily. The SDS of a chemical list known hazards and are good guidance on some safety practices but they do not tell the whole story. In order to assess if a chemical is safer, one needs to make sure that there is sufficient data available on multiple health endpoints that supports a claim of safer. Luckily, there are some positive lists being developed that help with this. One such list is the [EPA's Safer Chemical Ingredient List](#), which assesses chemicals against a broad range of

---

42. Adapted from the Decision logic for substances and mixtures hazardous to the aquatic environment, Decision logic 4.1.1 from Part 4 Environmental Hazards. Globally Harmonized System of Classification and Labeling of Chemicals (GHS) ("The Purple Book"), United Nations, 2005 First Revised Edition, 233–238.

potential toxicological effects. Each of the chemicals listed on the Safer Chemical Ingredient List meets the standardized criteria and might have additional restrictions it needs to meet depending on the reason the chemical is used.

### DOZN™ 2.0 Access and Scoring

DOZN™ 2.0 is a free open-access Green Chemistry tool provided by MilliporeSigma. The DOZN™ 2.0 approach to evaluating greener chemicals is based on the [12 Principles of Green Chemistry](#). These principles distill into three major categories: improving resource use, more efficient use of energy, and minimizing human and environmental hazards. At present, DOZN™ 2.0 does not incorporate lifecycle impacts of raw materials (ie. raw material extraction, pre-processing and manufacture), but does consider hazards of and the efficient use of such materials.

*Want to learn more about the methodologies behind DOZN™ 2.0? Check out the [publication for full details](#) or view the [DOZN™ 2.0 Webinar](#) for a breakdown from the Fellow & Global Manager of Green Chemistry at MilliporeSigma, Dr. Ettigounder Ponnusamy.*

### How to Access DOZN™ 2.0

To access the tool provide the requested information and register for a free account on the DOZN™ 2.0 website: <https://green.milliporesigmabioinfo.com/dozn/>. You will receive further email instructions to complete the registration.

### Specific rules for academic use of DOZN™ 2.0

- If the product is unknown the B score will be recorded as 1
- For energy considerations, mechanical grinding is not considered, nor is the heat generated by the reaction.
- If the duration of any reaction condition is not stated, an estimate based on a reasonable duration of the process should be used. For example, if one is filtering a 10mL solution via vacuum filtration a time of 10-20 minutes could be considered a reasonable duration.
- Water should be inputted such that its product number is 99053, brand is Sigma-Aldrich (default for all water), it is an auxiliary, and it is not considered a solvent.
  - Water is only considered a reactant when it is incorporated into the final product.
  - Water is considered an auxiliary when used as a source of H<sup>+</sup>

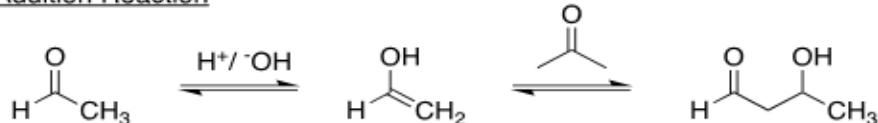
These rules and more have been developed into a word document template for using DOZN™ 2.0. This [template](#) can be adapted for use when conducting comparisons of reactions. Another resource that should be utilized before attempting to compare reactions using DOZN™ 2.0 is the [Employing DOZN™ 2.0 – The Quantitative Greener Alternative Evaluator in Academic Settings for Safer Labs Webinar](#) featuring Prof. Irv Levy explaining how his course utilized the tool and tip/tricks to help you adapt this resource to your needs.

## DOZN™ 2.0 Scoring Example

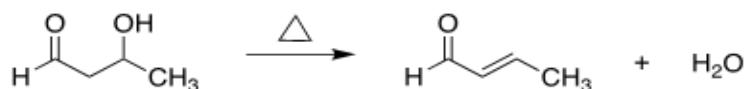
### *The Aldol Condensation Reaction*

One of the most powerful synthetic pathways to generate carbon-carbon bonds, a central focus in organic chemistry, is the aldol condensation. The aldol condensation reaction refers to a reaction in which an additional reaction between two molecules takes place, followed by loss of a small molecule such as water, carbon dioxide, or nitrogen gas.

#### Addition Reaction



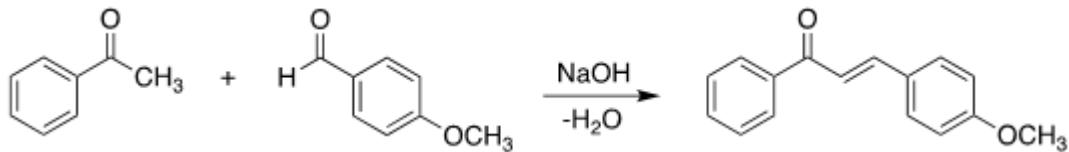
#### Elimination Reaction



An aldol possesses both an aldehydic group and a hydroxyl group, and hence the name aldol – *ald* for aldehyde, and *ol* for alcohol. When heated in acidic or basic conditions, the product of an aldol addition reaction will undergo elimination to yield an  $\alpha,\beta$ -unsaturated aldehyde or ketone with concomitant loss of water.

Below we will examine a traditional approach and greener solventless approach to the synthesis of trans-p-anisalacetophenone through DOZN™ 2.0 scoring.

### *Traditional Synthesis of trans-p-anisalacetophenone<sup>43</sup>*



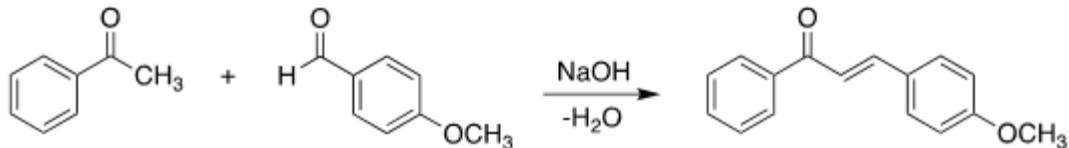

---

43. Preparation of trans-p-Anisalacetophenone, Experimental Organic Chemistry, 2011, 5th Edition, Gilbert and Martin, p. 620.

Chemical Name Sigma-Aldrich Catalog #	Information from SDS (2.1)	Information from SDS (10.6)	Information from SDS (12.1)
p-anisaldehyde A88107	Not a hazardous substance or mixture	<p>Hazardous decomposition products formed under fire conditions. - Carbon oxides</p> <p>Other decomposition products - No data available</p> <p>In the event of fire: see section 5</p>	No data available
Acetophenone A10701	<p>Flammable liquids (Category 4), H227</p> <p>Acute toxicity, Oral (Category 4), H302</p> <p>Eye irritation (Category 2A), H319</p> <p>Short-term (acute) aquatic hazard (Category 3), H402</p>	<p>Hazardous decomposition products formed under fire conditions. - Carbon oxides</p> <p>Other decomposition products - No data available</p>	<p>Toxicity to fish flow-through test LC50 - Pimephales promelas (fathead minnow) -</p> <p>162 mg/l - 96 h (OECD Test Guideline 203)</p> <p>Toxicity to daphnia and other aquatic invertebrates</p> <p>static test LC50 - Daphnia magna (Water flea) - 528 mg/l - 48 h</p> <p>Remarks: (ECHA)</p>

Chemical Name Sigma-Aldrich Catalog #	Information from SDS (2.1)	Information from SDS (10.6)	Information from SDS (12.1)
Water 99053	Not a hazardous substance or mixture.	No data available	No data available
Sodium hydroxide 221465	<p>Corrosive to metals (Category 1), H290</p> <p>Skin corrosion (Category 1A), H314</p> <p>Eye irritation (Category 2A), H319</p> <p>Short-term (acute) aquatic hazard (Category 3), H402</p>	<p>Hazardous decomposition products formed under fire conditions. - Sodium oxides</p> <p>Other decomposition products - No data available</p>	<p>Toxicity to fish LC50 - Gambusia affinis (Mosquito fish) - 125 mg/l - 96 h</p> <p>Remarks: (ECOTOX Database)</p> <p>Toxicity to daphnia and other aquatic invertebrates</p> <p>EC50 - Ceriodaphnia (water flea) - 40.4 mg/l - 48 h</p> <p>Remarks: (ECHA)</p>
Ethanol, 95% 459836	<p>Flammable liquids (Category 2), H225</p> <p>Eye irritation (Category 2A), H319</p>	<p>Other decomposition products - No data available</p> <p>Hazardous decomposition products formed under fire conditions. - Carbon oxides</p>	<p>Toxicity to fish flow-through test LC50 - Pimephales promelas (fathead minnow) - 15,300 mg/l - 96 h (US-EPA)</p> <p>Toxicity to daphnia</p>

			and other aquatic invertebrates  static test LC50 - Ceriodaphnia dubia (water flea) - 5,012 mg/l - 48h  Remarks: (ECHA)
Methanol 322415	Flammable liquids (Category 2), H225  Acute toxicity, Oral (Category 3), H301  Acute toxicity, Inhalation (Category 3), H331  Acute toxicity, Dermal (Category 3), H311  Specific target organ toxicity - single exposure (Category 1), Eyes, H370	Hazardous decomposition products formed under fire conditions. - Carbon oxides  Other decomposition products - No data available	Toxicity to fish flow-through test LC50 - Lepomis macrochirus (Bluegill) - 15,400.0  mg/l - 96 h (US-EPA)  Toxicity to daphnia and other aquatic invertebrates  semi-static test EC50 - Daphnia magna (Water flea) - 18,260 mg/l - 96 h  (OECD Test Guideline 202)
trans-p-anisalacetophenone S456748	No data available	No data available	No data available

*Traditional Synthesis of trans-p-anisalacetophenone<sup>43</sup>***Procedure:**

1. Dissolve 0.5 g of sodium hydroxide in 0.5 mL of water.
2. Place 0.2 mL of p-anisaldehyde and 0.2 mL of acetophenone in a conical vial containing a spinvane.
3. Add 0.7 mL of 95% ethanol and stir the contents of the vial to mix and dissolve the reactants.
4. Using a Pasteur pipet, transfer 2 drops of the sodium hydroxide solution into the reaction mixture.
5. Stir the reaction mixture at room temperature for 15 minutes. Then cool the reaction in an ice-water bath.
6. Collect the product by vacuum filtration, wash the product with 5-10 drops of cold 95% ethanol, and air-dry the crystals.
7. Recrystallize the crude product from 10 mL of methanol.
8. Obtain the mass of the product, determine the melting point, and analyze by melting point and NMR spectroscopy.

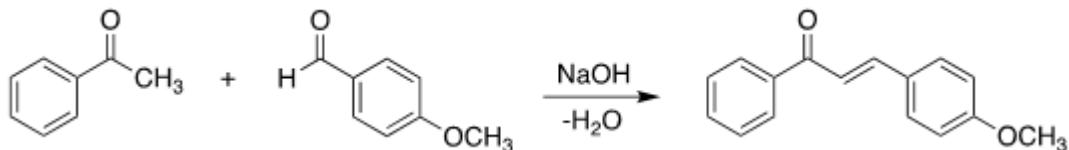
*DOZN™ 2.0 scoring:*

Remember the aggregate score gives a quick summary of the 12 principles, a snapshot of greenness. It is calculated by finding the total scoring of the three major groups: improved resource use, increased energy efficiency, and reduced human and environmental hazards. This number is then divided by 50. 50 is an arbitrary number to normalize the score to a 0-100 scale. The lower the aggregate score the greener the process.

Traditional Synthesis of trans-p-anisalacetophenone	
Principle	DOZN™ 2.0 Score
1.Prevention	25.0
2.Atom Economy	10.1
3.Less Hazardous Chemical Synthesis	11.1
4.Designing Safer Chemicals	2.0
5.Safer Solvents and Auxillaries	6.7
6.Design for Energy Efficiency	4.7
7.Use of Renewable Feedstocks	10.1
8.Reduce Derivatives	0.0
9.Catalysis	0.5
10.Design for Degradation	2.2
11.Real-time analysis for Pollution Prevention	1.0
12.Inherently Safer Chemistry for Accident Prevention	11.1
<b>Aggregate Score</b>	<b>0.4</b>

### *Greener Synthesis of trans-p-anisalacetophenone<sup>44</sup>*

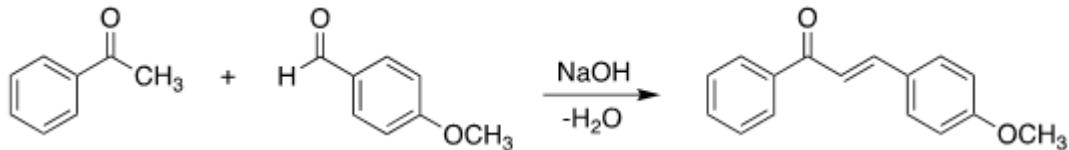
This is a solventless reaction, the reaction is promoted by grinding the reagents in a mortar and pestle.



Chemical Name Sigma-Aldrich Catalog #	Information from SDS (2.1)	Information from SDS (10.6)	Information from SDS (12)
p-anisaldehyde A88107	Not a hazardous substance or mixture	Hazardous decomposition products formed under fire conditions. - Carbon oxides Other decomposition products - No data available In the event of fire: see section 5	No data available
Acetophenone A10701	Flammable liquids (Category 4), H227 Acute toxicity, Oral (Category 4), H302 Eye irritation (Category 2A), H319 Short-term (acute) aquatic hazard (Category 3), H402	Hazardous decomposition products formed under fire conditions.  Carbon oxides Other decomposition products - No data available	Toxicity to fish flow-through test LC50 - Pimephales promelas (fathead minnow)  162 mg/l - 96 h (OECD Test Guideline 203)  Toxicity to daphnia and other aquatic invertebrates  static test LC50 - Daphnia magna

44. Palleros, D. R. Solvent-free Synthesis of Chalcones. *J. Chem. Educ.*, **2004**, 81, 1345.

			(Water flea) - 528 mg/l - 48 h Remarks: (ECHA)
Water 99053	Not a hazardous substance or mixture.	No data available	No data available
Sodium hydroxide 221465	Corrosive to metals (Category 1), H290 Skin corrosion (Category 1A), H314 Eye irritation (Category 2A), H319 Short-term (acute) aquatic hazard (Category 3), H402	Hazardous decomposition products formed under fire conditions. - Sodium oxides Other decomposition products - No data available	Toxicity to fish LC50 - <i>Gambusia affinis</i> (Mosquito fish) - 125 mg/l - 96 h  Remarks: (ECOTOX Database)  Toxicity to daphnia and other aquatic invertebrates  EC50 - <i>Ceriodaphnia</i> (water flea) - 40.4 mg/l - 48 h Remarks: (ECHA)
Ethanol, 95% 459836	Flammable liquids (Category 2), H225 Eye irritation (Category 2A), H319	Other decomposition products - No data available  Hazardous decomposition products formed under fire conditions. - Carbon oxides	Toxicity to fish flow-through test LC50 - <i>Pimephales promelas</i> (fathead minnow) - 15,300 mg/l - 96 h (US-EPA)  Toxicity to daphnia and other aquatic invertebrates  static test LC50 - <i>Ceriodaphnia dubia</i> (water flea) - 5,012 mg/l - 48h Remarks: (ECHA)
trans-p-anisalacetophenone S456748	No data available	No data available	No data available

*Greener Synthesis of trans-p-anisalacetophenone<sup>44</sup>***Procedure:**

1. To a 3-inch porcelain mortar, add 0.6 mL p-anisaldehyde, 0.6 mL of acetophenone, and 200 mg of solid sodium hydroxide. Grind with the pestle for 5-10 minutes. The mixture may quickly become pasty. Continue grinding until the mixture solidifies and breaks into small particles.
2. Add 10 mL distilled water and mix with the pestle and a spatula to dislodge the solid from the wall of the mortar.
3. Obtain the solid via suction filtration using a Buchner funnel. Rinse the mortar and pestle with 5 mL water and collect the rinses on the same filter.
4. Wash the product on the filter with an additional 5 mL water and allow to dry.
5. Recrystallize the crude product from 10mL of 95% ethanol.
6. Obtain the mass of the product, determine the melting point, and analyze by melting point and NMR spectroscopy.

**DOZN™ 2.0 scoring:**

Greener Synthesis of trans-p-anisalacetophenone	
Green Chemistry Principle	DOZN™ 2.0 Score
1.Prevention	15.7
2.Atom Economy	24.0
3.Less Hazardous Chemical Synthesis	25.0
4.Designing Safer Chemicals	2.0
5.Safer Solvents and Auxillaries	1.3
6.Design for Energy Efficiency	7.5
7.Use of Renewable Feedstocks	24.0
8.Reduce Derivatives	0.0
9.Catalysis	1.0
10.Design for Degradation	2.0
11.Real-time analysis for Pollution Prevention	1.0
12.Inherently Safer Chemistry for Accident Prevention	25.0
<b>Aggregate Score</b>	<b>0.6</b>

### *DOZN™ 2.0 Score Discussion*

To properly compare each procedure, each score for the 12 principles of Green Chemistry should be evaluated. The greener procedure shows an improvement in the prevention of waste (principle 1) and safer solvents and auxiliaries (principle 5). The greener procedure does not show an improvement in principles: 2, 3, 6, 7, 12. When comparing these two procedures, the most probable cause of an increase in DOZN™ 2.0 score is the increase in use of auxiliaries between the two procedures. An auxiliary is anything other than a reactant (e.g. a washing solution or non-reacting solvent), the auxiliaries do not become incorporated into the final product and therefore are considered as waste unless it is recovered and reused. The traditional procedure contains 2.133 g of auxiliaries, if one assumes 10 mL of methanol is used for the recrystallization of .267 g product. While the greener procedure contains 21.18 g of auxiliaries, if one assumes 10 mL of ethanol used for recrystallization of 0.937 g of product. Therefore, the greener procedure produces more waste.

To improve the analysis of the greener procedure, a suggestion is made to reduce the amount of water. We consider water to be a greener solvent, however we must consider that the aqueous waste from this reaction will contain a small amount of organic material and therefore is considered hazardous waste that must be incinerated. If the amount of water were decreased by half most of the twelve principles would be improved from the traditional microscale reaction. This degree of improvement would not be observed if the amount of water used was decreased by one third. This suggests the amount of water used in the procedure should be decreased by half (if chemically possible) to improve the overall greenness of the greener procedure. Of course, an improvement in all twelve principles would be preferred but by allowing students to see an improvement in most of the twelve principles, it will be clear that the new greener procedure is overall better than the traditional procedure. This may also provide the opportunity for the students to compare each procedure to determine why each principle improved in the greener procedure. For example, a decrease in both principle 3 and 12 is due to both a decrease in the amount of solvent (compared to the original greener procedure) and a decrease in the hazard of the auxiliary (water vs. ethanol). Overall, allowing students to see a decrease in DOZN™ 2.0 score (increase in “greenness”) may allow each of the twelve principles of Green Chemistry to be better examined.

Principle	Traditional Procedure	Greener Procedure with Half Water Use	Greener Procedure with 2/3 Water Use
1. Prevention	25.0	9.10	10.67
2. Atom Economy	10.1	11.84	14.99
3. Less Hazardous Chemical Synthesis	11.1	12.84	15.99
4. Designing Safer Chemicals	2.0	2.00	2.00
5. Safer Solvents and Auxiliaries	6.7	1.20	1.18
6. Design for Energy Efficiency	4.7	3.48	4.53
7. Use of Renewable Feedstocks	10.1	11.84	14.99
8. Reduce Derivatives	0.0	0.00	0.00
9. Catalysis	0.5	1.00	1.00
10. Design for Degradation	2.2	2.02	2.01
11. Real-time analysis for Pollution Prevention	1.0	1.00	1.00
12. Inherently Safer Chemistry for Accident Prevention	11.1	12.84	15.99

### *Conclusions*

Due to the assumptions made during the analysis of a reaction it is not expected that students will arrive at the exact same DOZN™ 2.0 for a given reaction. Therefore, the process to arriving at the DOZN™ 2.0 score should be considered by the instructor rather than a direct match to a given set of values. This allows the instructor to investigate a student's understanding of chemical reactions and the process by which they approach the analysis of the reaction and data entry into the DOZN™ 2.0 software.

For more tips and tricks as well as ideas on how to implement this tool and resource in your course view the [Employing DOZN™ 2.0 – The Quantitative Greener Alternative Evaluator in Academic Settings for Safer Labs Webinar](#) featuring Prof. Irv Levy explaining how his course utilized the tool.

This guide has many examples of how to practice green chemistry, however, simple changes to your everyday practices can result in greener lab work. Check out the resource created by the [Green Chemistry Initiative at the University of Toronto](#) and post this in the lab as a reminder that small steps make an impact. [Access a copy here!](#)

## Simple Techniques to Make Everyday Lab Work Greener

### Solvent Selection

#### 1 Use dry ice/isopropanol for cooling baths

Reaches essentially the same temperature as dry ice/acetone (-77°C vs. -78°C), but the lower volatility of isopropanol minimizes vapor emissions and inhalation, and makes the bath last longer.

#### 2 Use heptane instead of hexanes

Heptane has almost identical chemical properties to hexane, but is significantly less toxic due to the odd number of carbons, which alter its metabolic product in the body.

#### 3 Use 2-MeTHF instead of THF

2-MeTHF is indirectly derived from bio-based renewable feedstocks. Its chemical properties are very similar to THF but it is immiscible with water, making separations, recycling, and drying easier. See D. F. Aycock, *Org. Process Res. Dev.* 2007, 11, 156–159 for more information.

#### 4 Substitute DCM in column chromatography

One of the largest contributors to chlorinated solvent waste is chromatography. While selecting a new solvent system may seem challenging, J. P. Taylerly, et al. (*Green Chem.* 2012, 14, 3020-3025) have already done the work for you.

### Waste Reduction

#### 5 Recycle wash solvents

Wash solvents are ideal for recycling because dryness and purity isn't as important. Simply wash your glassware as usual, collecting the liquid in a separate container. When it's full, transfer to the rotovap and distill into a clean collection flask.

#### 6 Recycle solvents isolated from distillation/rotovaping

If you are going to remove the solvent anyway, why not reuse it? When you are done your purification step, do a quick check of the purity of the solvent. If pure: reuse it for another reaction or as a wash solvent. This is ideal for single-solvent systems, azeotropes, and solvent mixtures with >10°C difference in boiling point.

#### 7 Use a closed-loop cooling system for condensers

Closed-loop cooling systems eliminate wastewater and accidental laboratory flooding. Use a commercially available chilled water recirculator, an aluminum condenser, or for high-boiling liquids simply use air.

#### 8 Use Dry Column Vacuum Chromatography to purify large samples

This is a relatively new technique that can dramatically reduce the amount of silica and solvents used. For larger purifications, it's faster than flash chromatography and the columns can easily be recycled. For more information see D. S. Pedersen and C. Rosenbohm, *Synthesis* 2001, 16, 2431-2434.

### Energy Reduction

#### 9 Close your fume hood

A variable volume fume hood is 60% more energy efficient when the sash is closed.

#### 10 Turn off/unplug stuff when you are done with it

It just makes sense.

This document was prepared by:

