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Choose Your Own (Green) Adventure: A Solventless Aldol Condensation Experiment for the Organic Chemistry Laboratory

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Abstract Aldol condensation reactions are routinely used in organic chemistry teaching labs. In this experiment, we developed a greener method for the aldol condensation experiment of the Organic Chemistry II lab at North Carolina State University. To do this, we used the 12 Principles of Green Chemistry, and altered our current procedure to fit as many of them as possible. The main approach used throughout this process was developing aldol condensation reactions that were completely solventless. We currently have a procedure that allows for all possible combinations of two aldehydes: 4-tolualdehyde and 4-anisaldehyde, and two ketones: acetophenone and 4-methylacetophenone. We have developed a method that not only reduces solvent consumption, but also qualifies under 5 other green chemistry principles: prevention of waste, less hazardous chemical synthesis, reduction of derivatives, accident prevention, and atom economy. This new experimental design allows students to choose the compounds they would prefer to use from a list of available reagents therefore allowing a certain degree of lab personalization.

Keywords: *green chemistry, sophomore organic lab, aldol condensation, solventless reactions*

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1. Introduction

Green Chemistry is a rapidly growing discipline aimed at designing chemical reactions and products that reduce the production of hazardous substances. [1] The twelve principles of green chemistry lay the foundation for this goal and must be utilized at all opportunities to maximize the greenness of the desired reaction. The current method of thinking about Green Chemistry was developed in 1987 from the United Nations Commission on Environment and Development. This commission defined sustainable development as “...meeting the needs of the present without compromising the ability of future generations to meet their own needs.” [2] This commission paved the way to the development of the 12 principles of green chemistry, laid out below. [1]

2. Principles of Green Chemistry:

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

In recent years, the greening of organic chemistry teaching labs has been well underway, with numerous publications and presentations at conferences involving new lab experiments that incorporated the principles of green chemistry. [3] From alkene isomerization to reduction of a ketone to oxidation of alcohols, many experimental methods have been developed to alter the organic chemistry labs. [2] Even acylation reactions, such as lidocaine synthesis, have been modified to implement green chemistry. [4] Green Chemistry doesn’t just have application in organic chemistry though, it can apply to nanotechnology and even into industry. [5,6] Introducing the principles of green chemistry into teaching or industrial labs is said to have many benefits beyond just environmental. One study noted that integrating green chemistry into teaching labs at an introductory collegiate level lead to an increase in students’ passion for both chemistry and the green movement. [6]

Aldol condensation reactions have been studied extensively, as they are one of the most significant general methods for the formation of carbon-carbon bonds in organic chemistry. [7] This reaction is a common experiment done in a sophomore level organic chemistry lab. While many researchers have aimed to integrate green chemistry into the aldol reaction, they have typically come with a major drawback, such as high hazards or high waste production. [8] Palleros (2004) published a comprehensive paper in the Journal of Chemical Education that provided several examples of this reaction. [9] From this, we aimed to produce a practical resource to use within an undergraduate teaching lab.

We have been interested in the incorporation of green experiments in our organic chemistry lab curriculum. [10] In this experiment, modifications have been made to the traditional aldol condensation used in labs on campus, in order to make it greener. These changes result in a faster reaction time (when compared to the traditional procedure), an elimination of the need for a solvent, a reduction in the amount of waste produced, and a simpler reaction procedure. [9,11] The modifications fulfill six of the twelve principles of Green Chemistry: prevention of waste, reduction of derivatives, safer solvents and auxiliaries, safer chemistry for accident prevention, less hazardous chemical synthesis, and maximization of atom economy.

3. Experimental

3.1. Reagents Used

The following chemicals were utilized in this experiment: 4-tolualdehyde, 4-anisaldehyde, 4-methylacetophenone, acetophenone, and sodium hydroxide pellets, as well as a 10% aqueous HCl solution. Reagents were purchased from Sigma-Aldrich and Fisher Scientific and used without further purification.

3.2. Procedure

This procedure is written for all possible combinations of the 2 aldehydes and 2 ketones previously mentioned in the **Reagents Used** section. Using a volumetric pipet, 0.50 mL of the selected aldehyde and 0.40 mL of the selected ketone were added to a mortar. Approximately 0.10 g of solid NaOH was added to the reaction and then using a pestle, was crushed up within the solution. The reaction was ground until the formation of a solid was observed. After the solid began to form, the mixture was allowed to sit for 10 minutes, to ensure completion. Once the 10 minutes had passed, 2 mL of 10% aqueous HCl were added to neutralize any residual NaOH. This mixture was then allowed to sit for an additional 10 minutes, before vacuum filtration was performed. The sample was washed with a small amount of cold 90% ethanol.

3.3. Hazards

The use of proper personal protective equipment, such as eye protection, by researchers was required at all times in the laboratory. Ethanol was handled with caution due to flammability. Both aldehydes (4-anisaldehyde and 4-tolualdehyde) are air sensitive, so the containers were covered with parafilm to avoid contamination. In addition to this, the reagents used are eye, skin, and respiratory irritants and were dispensed within a fume hood. Used solvents and filtrate were disposed of in the organic unwanted liquid material container, while solid product was disposed of in the organic unwanted solid material container.

4. Results and Discussion

This experiment was designed to offer a green alternative to traditional aldol condensation reactions within a second semester organic chemistry lab. Introducing a procedure that incorporates several principles of green chemistry, such as reduced auxiliaries, atom economy, and waste reduction, could be beneficial to students. The traditional procedure requires students to combine acetone and acetophenone with a 1:1 95% ethanol: 3M sodium hydroxide solution in an Erlenmeyer flask. The students then stir intermittently for 15 minutes, isolate the product, and recrystallize. This procedure leads to low yields and impure products (as determined through melting point analysis). [11] The proposed procedure will require students to mix one of two aldehydes (4-tolualdehyde or 4-anisaldehyde) with one of two ketones (acetophenone or 4-methylacetophenone) in the presence of a pellet of sodium hydroxide in a mortar. The students then grind the solution until a solid is observed. Next, they use a small amount of 10% HCl to neutralize the product, followed by filtering and washing with cold 90% ethanol. No recrystallization was necessary with these products as they have moderate to high purity based on IR spectroscopy and melting point analysis, with the exception of the combination of anisaldehyde and acetophenone, which did not react.

Table 1 shows the three combinations of aldehydes and ketones that were tested in this experiment. These combinations (options 1-3) are then compared to the traditional aldol reaction done with benzaldehyde and acetone in Table 2.

Table 2 below shows a comparative analysis of the greenness of the two procedures. The comparison was limited to the 6 principles of green chemistry that the proposed procedure enhanced from the prior method.

Table 1. Combinations of aldehydes and ketones tested for green aldol condensation reaction

Option Number	Aldehyde	Ketone	Avg. % Yield
1	4-tolualdehyde	4-methylacetophenone	82%
2	4-anisaldehyde	4-methylacetophenone	93%
3	*p*-tolualdehyde	acetophenone	78%

Table 2. Comparative analysis of a current and the proposed procedures for an aldol condensation reaction

Green Chemistry Principle Utilized	Before Alterations were Made	After New Procedure was Developed
Safer Solvents	EtOH/NaOH solution	No solvent
Prevention of Waste	Produces 5-10 mL of waste per group	Produces 2-5 mL of waste per group
Less Hazardous Chemical Synthesis	Reagents are flammable, irritants, harmful if swallowed, and corrosive.	Reagents are labeled as irritants. Solid NaOH poses less of a risk for spill than solution.
Reduction of Derivatives	Can produce the desired solid as well as an oil	Produces the desired product (trans)
Accident Prevention	Harsh chemicals used by relatively inexperienced chemists.	Less likelihood of a spill with no solvent. Less harsh chemicals
Atom Economy	Typical Values: 28% Crude 3% Recrystallized	Average Values: 81-91%

As seen in Table 2, the proposed method offers many green benefits when compared to the current one, such as the elimination of solvent, reduction of waste and derivatives, curtailment of hazardous risks, improvement of atom economy, and enhancement of accident prevention. An additional benefit of the proposed procedure is that with the multiple choices and reduction of reaction time, students are able to synthesize more than one product, thus giving them more practice with the various techniques used. Students also have more time to analyze the IR spectra and melting point data to determine the relative purity of the product.

5. Conclusion

The aldol condensation is a very useful reaction in organic chemistry for its ability to form carbon-carbon bonds; it is also a relatively simple procedure in use in many teaching labs. Some current methods tend to result in low yields and purity. In this experiment, we redesigned this method to enhance the green chemistry aspect of the reaction and increased the number of possible reagents in order to give students a degree of choice when completing the experiment. The modifications of the experiment to meet the principles of green chemistry resulted in a new procedure that not only produced high yields and purity, but also eliminated the use of solvents, reduced derivative formation, reduced chemical risks, increased atom economy, and decreased the chance of accidents.

Acknowledgments

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