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A greener method for the Diels-Alder reaction using anthracene and maleic anhydride

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ABSTRACT

As modern society continues to develop and look for change in our current habitation conditions, it seems to be a necessity to begin searching for various new methods in industrial performance and scientific methods to provide greener alternatives. Various chemical industries use many organic syntheses to produce important biological molecules, drugs, fragrances, agrochemicals, and pharmacological products. In industry, there are numerous varieties of solvents being used in production processes that lead to the eventual waste of these chemical substances. One reaction that is prevalent in these industries is the Diels-Alder reaction. The Diels-Alder reaction is a common laboratory that we often see in the undergraduate organic chemistry laboratory curriculum. The most common Diels-Alder synthesis in laboratory manuals uses xylene as the solvent in the reaction between anthracene and maleic anhydride. However, xylene is a high-boiling, toxic, aromatic solvent. This study focuses on developing a greener method for the Diels-Alder reaction that is carried out in undergraduate organic chemistry labs. Different solvents and reaction times were evaluated to replace xylene as the solvent. The results suggest that crude product yields were slightly lower than the controls with the use of ethyl acetate and ethanol with a reaction time of sixty minutes. However, the melting point ranges produced by the varied experimental conditions did not produce the expected range of the desired product, so the use of ethyl acetate and ethanol as good replacements for xylene cannot be confirmed without further analysis of the crude final product.

Keywords: *Diels-Alder, anthracene, maleic anhydride, xylene, ethyl acetate, ethanol*

INTRODUCTION

The field of green chemistry is becoming a forefront of modern-day scientific research. Green chemistry is defined as the ‘‘design of chemical products and processes to reduce or eliminate the use and generation of hazardous substances,’’ (Anastas & Eghbali, 2009). Green chemistry made its introduction as a field of study with the collective research of environmentally friendly studies in the early 1990s (Horvath & Anastas, 2007). As this field of research has been developed, twelve core principles of green chemistry have arisen. In 1998, Paul Anastas and John Warner created the twelve principles of green chemistry that are being used in modern times to frame many newly developed chemical reactions and developments (Anastas & Eghbali, 2009). Some of these principles include, “it is better to prevent waste than to treat or clean up waste after it is formed. Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment and substances and the form of a substance used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires,” (Poliakoff *et al*., 2002). With the development of green chemistry, not only can industrial waste in organic synthesis be minimized, but organic synthesis in a general sense can undergo waste reduction as well.

As the Earth seems to be struggling in recent years with toxic waste levels, applying green chemistry principles to organic synthesis is becoming an extremely important process. In modern day society, over 98% of all organic chemicals are developed and produced from refined petroleum, which is extremely harmful to the environment (American Chemical Society 2020). Also, in a study done on the effect of organic chemicals on the Earth’s water supply, 14% of chosen monitoring sites were affected by organic chemical waste and 42% of the sites had the potential of being affected by the hazardous waste (Malaj *et al*., 2014). In regard to organic synthesis methods in industry, commercial manufacturers are using over 15 billion kilograms of solvents yearly, which are used extensively in production methods and give off numerous amounts of chemical waste into the environment (Shanab, Neudorfer, Schirmer, *et al.*, 2013). With all of the waste and potential waste products being produced by organic synthesis, it is vital to develop greener methods of organic syntheses to cut down on the harmful tolls being taken on the environment.

There are multiple aspects of an organic synthesis that can potentially be manipulated in order to produce less toxic waste products. One larger factor that leads an organic reaction to be “less green” is the solvent being used, a solvent being a liquid used to dissolve other substances. In the past fifteen years, many solvent alternatives have been studied to replace currently toxic solvents, those being water, fluorous solvents, ionic liquids, organic carbonates, carbon dioxide, and biosolvents (Shanab, Neudorfer, Schirmer, *et al.*, 2013). Another aspect of an organic reaction that can be manipulated is the use of catalysts, which are substances that increase the rate of a chemical reaction without undergoing a permanent chemical change. In looking for an ideal catalyst, some preferable characteristics include a catalyst that produces a large product yield per one molecule of the catalyst, one that does not deactivate or poison during the reaction, is readily available and inexpensive, and need not require an initiation step for activation (Gladysz, 2001). Many other aspects of an organic synthesis can be manipulated, such as reactants, energy input (in terms of heating and cooling), and environmental conditions of the reaction itself. When performing an organic synthesis, it is important to evaluate all factors of the reaction in green chemistry and adjust them accordingly in order to decrease the overall waste output of the reaction.

Because of the toxic conditions that come with organic synthesis, green chemistry must be more readily applied to organic chemistry, and in particular, organic chemistry laboratories in student education. Green chemistry is already being applied and evaluated in an industrial sense, but many secondary educational programs use harmful organic reactions in laboratories every year in order to learn organic chemistry techniques. With students using “nongreen” techniques to perform these organic reactions, much energy waste and waste products are produced when taking the whole secondary education system together across the world. Overall, it is important to evaluate these organic synthetic methods for greenness and to adjust the reactions to assist in lower toxicity levels of teaching organic synthesis.

There are many reactions taught at the basic levels of organic chemistry, broadly including substitution, elimination, and addition reactions. The Diels-Alder reaction is a common organic synthesis taught in undergraduate laboratories. It was developed in 1928 by Otto Diels and Kurt Alder which is very useful in the synthesis of polycyclic organic products and is known for its particular regioselectivity and stereoselectivity in its products (Brieger & Bennett, 1980). A Diels-Alder reaction most commonly occurs between a diene [a hydrocarbon containing two double bonds] and an α, β -unsaturated carbonyl compound, a diene having a low ionization potential and the carbonyl being highly electrophilic (Woodward, 1942). Keeping the properties of the Diels-Alder reaction in mind as well as the idea of green chemistry, it is important to understand that any reaction has the potential of being made more environmentally friendly. By manipulating multiple aspects of a Diels-Alder reaction such as solvent use, catalyst use, energy production and consumption, and environmental conditions of the reaction, the Diels-Alder reaction has the potential of becoming a greener reaction and could produce less toxic waste in experimentation.

In addition to being taught in undergraduate organic chemistry laboratories across the globe as a pericyclic reaction example, the Diels-Alder reaction also has other significances and uses. The Diels-Alder reaction is not used very commonly in industry but is generally used as a key step to preparing complex molecules that are of importance in the biological industry (Gilbert & Martin, 2002). Interestingly, nature also takes advantage of the Diels-Alder reaction in the preparation of compounds that occur in living organisms (Gilbert & Martin, 2002). The Diels-Alder reaction has also been known to be used in the synthesis of fragrances, agrochemicals, active pharmacological ingredients, and flavoring products (Funel & Abele, 2013). In this study, solvents and reaction times will be altered in order to determine whether the standard reaction between anthracene and maleic anhydride can become greener.

MATERIALS AND METHODS

To ensure no contaminants or impurities are present on the glassware between trials, it was washed in a base bath, followed by an acid wash. For the base bath, two gallons of 70% isopropyl alcohol were combined with potassium hydroxide. The glassware was allowed to soak in the base bath for 3-4 hours. After soaking in the base bath, the glassware was rinsed with tap water, followed by rinsing with deionized water. After rinsing with water, the glassware was washed with 3.0 N hydrochloric acid. Following the acid rinse, the glassware was rinsed with deionized water and placed in the oven at 105°C to dry overnight.

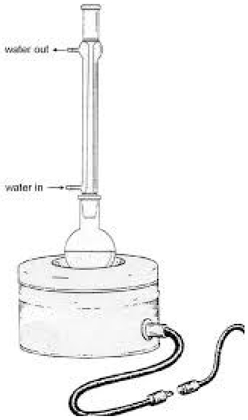

Figure 1. Single reflux apparatus set-up using an electric flask heater. (University of Calgary Chemistry Department)

Using the procedure outlined by L. G. Wade, Jr. of Whitman College, three samples of 0.5 grams of Anthracene and three samples of 0.25 grams of Maleic Anhydride were weighed out using an analytical balance. Each 0.5 g sample of anthracene and each 0.25 g sample of maleic anhydride were placed into three separate 100 mL round-bottom flasks. 6 mL of xylene were dispensed to each of the round bottom flasks using a 10 mL pipet and a pipet dispenser. A stir bar was also added to each reaction flask. Reflux apparatuses were assembled according to Figure 1.

Three repetitions of each reaction were carried out according to Figure 2. The reaction mixtures were refluxed for thirty minutes while stirring. Once the reaction flasks were cooled to room temperature, each flask was placed in an ice water bath and chilled for five minutes to maximize crystallization.

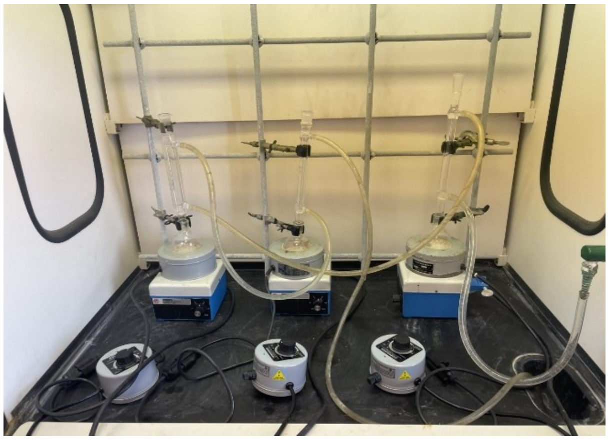

Figure 2. Reflux apparatus set-up in order to perform three reactions simultaneously.

The crude product was collected using vacuum filtration with a Büchner funnel and adapter, as shown in Figure 3. Each of the crude products were washed with 3 mL of ice-cold xylene.

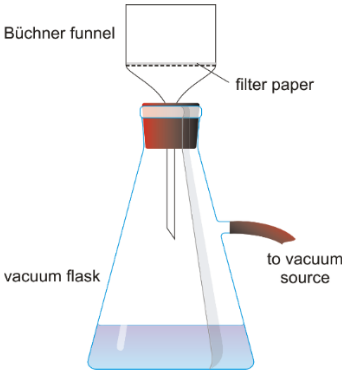

Figure 3. Vacuum Filtration set-up using a vacuum flask, Büchner Funnel, and adapter (Generalic, 2020).

In order to dry the products, the filter paper with crystals was transferred onto a watch glass. The crude products were placed in an oven at 105°C to dry overnight.

The crude products were weighed using an analytical balance and the melting points (m.p.) were obtained using an SMP10 digital melting point apparatus. Each was placed in a 3 mL product vial and sealed with Parafilm until recrystallization to ensure moisture did not tamper with the product. This experiment is considered as the control due to two reasons, the first being that this is the standard procedure in undergraduate lab texts and the second being that all changes to the experimental procedure will be compared to this control procedure.

The above process was repeated using the solvents ethyl acetate, ethanol, and water, as a replacement of xylene with the different reaction times given in Table 1.

Table 1. Experimental conditions varied from the standard procedure (defined as the control).

Experimental Condition	Solvent	Reflux Time (min.)
A	Xylene	30
B	Ethyl Acetate	30
C	Ethyl Acetate	60
D	Ethanol	30
E	Ethanol	60
F	Water	30

In an evaluation of the efficiency of the other solvents as recrystallizing solvents, 0.2 grams of each crude product were recrystallized using three different solvents, xylene (as in the standard procedure), ethyl acetate, and ethanol, separately.

Each of the products were placed in an oven heated to 105°C to dry overnight. After drying, each product was collected and weighed using an analytical balance. The melting points of the recrystallized products were then taken using an SMP10 digital melting point apparatus.

RESULTS

According to the crude product experimental data (table 2), the control had a percentage yield of 67.39% on average. The crude melting points of the control products were in the range of 262°C-264°C which is in the acceptable m.p. range of 9,10-dihydroanthracene-9,10-α, β-succinic anhydride, 260°C-263°C.

In an analysis of the crude products of experimental conditions B-E, each of the percentage yields were lower than that of the controls (table 2). The crude melting point ranges of each of the experimental conditions were lower than the range of the desired product as well (Table 2).

Table 2. Comparison of crude product average percentage yields and average melting point ranges under each experimental condition.

Solvent	Reflux Time (min.)	Average Percentage Yield (crude)	Average M.P. Range (°C)
Xylene	30	67.39	262-264
Ethyl Acetate	30	57.12	216-218
Ethyl Acetate	60	54.79	219-221
Ethanol	30	43.56	217-219
Ethanol	60	58.11	217-219
Water	30	0	N/A

Upon recrystallization, the melting point ranges of experimental conditions A-E were not affected by the recrystallizing solvents (Table 3). Water was excluded from the analysis as it did not produce a crystallized product.

Table 3. A comparison of melting point ranges across recrystallizing solvents.

Experimental Solvent	Time (min.)	Recrystallizing Solvent	M.P. Range (°C)
Xylene	30	Xylene	262-246
		Ethyl Acetate	262-264
		Ethanol	262-264
Ethyl Acetate	30	Xylene	218-220
		Ethyl Acetate	218-220
		Ethanol	218-220
Ethyl Acetate	60	Xylene	219-221
		Ethyl Acetate	218-220
		Ethanol	217-219
Ethanol	30	Xylene	217-219
		Ethyl Acetate	217-219
		Ethanol	219-221
Ethanol	60	Xylene	218-220
		Ethyl Acetate	218-221
		Ethanol	217-220

In an analysis of the recrystallizing solvents, ethanol had the largest percent recovery of its product compared to xylene and ethyl acetate (Table 4). However, these results cannot present significance until further analysis of the product is conducted.

Table 4. Average percentage recovery attained by each recrystallizing solvent.

Recrystallizing Solvent	Average Percent Recovery
Xylene	57.85
Ethyl Acetate	53.37
Ethanol	75.92

DISCUSSION

In terms of the control products (A), each of the controls had a m.p. range that was in the accepted range of the desired product. All variations of solvent and time condition in experimental conditions B-E produced consistently lower m.p. ranges than the desired product and the controls. However, the m.p. ranges of experimental conditions B-E were slightly higher than the range of pure anthracene and pure maleic anhydride, 215°C and 52.8°C, respectively. This suggests that each of the experimental conditions B-E produced a similar product, but products that were different than the desired product of the Diels-Alder reaction between anthracene and maleic anhydride.

In terms of product analysis, further research must be conducted in order to determine the identity of products B-E. The specific product of the controls has yet to be determined by Infrared spectroscopy (IR) and Nuclear Magnetic Resonance Spectroscopy (NMR) but was assumed to be 9,10-dihydroanthracene-9,10-α, β-succinic anhydride as the control m.p. ranges were in the desired range of the product.

The Diels-Alder reaction between anthracene and maleic anhydride is usually a thermal reaction, involving the breaking of three pi bonds, and the formation of two sigma bonds and one new pi bond. This reaction requires energy in order to start the reaction, but the overall reaction should be exothermic due to the formation of the two sigma bonds and the new pi bond. In the standard reaction, xylene is used as a high-boiling solvent in order to drive a quicker reaction. However, with changing the solvent to a lower-boiling and more green solvent such as ethyl acetate or ethanol, perhaps the solvent did not produce enough energy in reflux to insight the reaction fully. Experimental conditions C and E using a 60-minute time condition produced promising yields, but not of the desired product. This result possibly suggests that with the lower boiling solvents, more thermal energy is required to insight a full reaction between anthracene and maleic anhydride. Further analysis of the crude products must be conducted in order to determine if ethyl acetate and ethanol would be suitable solvents to carry out the desired reaction of the starting materials.

In recrystallization, it is notable that the m.p. ranges did not change from the crude product to the recrystallized product in each of the experimental conditions. This result suggests that the crude products were relatively pure and perhaps that recrystallization was not necessary and could be a step to be eliminated to produce a greener outcome, using less xylene than originally called for in the standard reaction. However, more research of each of the crude products must be conducted to confirm this result.

Overall, even though McPherson College cannot replace the current undergraduate laboratory method of the Diels-Alder reaction between anthracene and maleic anhydride with a greener solvent, this specific study did not purchase any new chemicals in order to carry out the analysis. This suggests that this specific study produced a greener outcome because there was no purchase of new chemicals to add to McPherson College's stock room, only the use of preexisting chemicals. Further research will be conducted on this study in order to determine the identity of the products produced by the varied experimental conditions and aims to be able to determine a greener alternative to the current undergraduate teaching laboratory method in the future.

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