Oxidation of Indanol to Indanone Through the Optimization of Various Parameters of Microwave Irradiation

Abstract

This study explored indanol oxidized to indanone using microwave irradiation under varying parameters of time and temperature with a constant wattage. The oxidizing agent used was chromium trioxide resin (polymer-supported chromic acid) in dichloromethane as the solvent. After 24 reactions were completed, the software, Minitab, was used to determine whether time or temperature, or whether both parameters together, influenced percent conversion of indanol to indanone. Percent conversion was determined by analyzing ^{1}H NMR of each of the reactions. The data showed that both temperature and time had an effect on the amount of indanol converted to indanone, with increasing temperature and time demonstrating an increase in percent conversion.

Introduction

a. Microwave Assisted Synthesis

Microwave assisted synthesis was first used in 1955 by Tappan, however, the domestic use of microwave ovens became more popular during the 1970s and 1980s[1]. There are several types of microwave reactions included microwave assisted reactions using solvents, microwave assisted reactions under solvent free conditions, microwave assisted reactions using solid phase, and microwave assisted reactions on mineral supports in dry media[1]. There are many advantages to microwave synthesis reactions including increased reaction rate with less usage of energy for chemical reactions, high efficiency and uniform heating, selectivity of chemical with improved reproducibility, reduced reaction time with yield and purity of product, and more[1]. This reaction type is especially important in the drug discovery and development process.

b. Theory Behind Microwave Assisted Synthesis

Microwaves fall on the electromagnetic spectrum at 10^{-2} meters which lies between radio waves and infrared waves[1]. Microwaves consist of an electric field and a magnetic field. The electric field is what transfers the energy into the reaction which heats it up and causes a sudden rise in temperature[1]. When the microwave energy pass through the samples, it causes the ions and molecules to oscillate[1]. Solvents and reagents uniquely absorb the microwave energy. The use of microwaves lead to an increase in reaction rates and also increases yields[1].

c. Solvents in Microwave Organic Synthesis

Solvents can be an effective tool in microwave oxidation if used property. When a solvent is more polar, it has greater efficiency with microwave energy. The solvent used in this experiment was dichloromethane, which exhibits this polar property.

d. Microwave Assisted Oxidation of Secondary Alcohols

Secondary alcohols can be oxidized to ketones and using microwave irradiation may assist this process efficiently. Many studies have incorporated the oxidation of secondary alcohols to their respective ketones.

e. Chromium Trioxide Resin as a Reagent

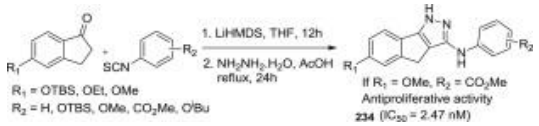
Chromium Trioxide is a common reagent used in the oxidation of secondary alcohols, however, when supported on polymeric resin, it becomes less toxic and more

environmentally friendly. This reagent enhances the reactivity and allows for greater percent yields to be achieved.

f. Importance of Indanone

Indanone comes in the form of white crystalline flakes. It has a molecular weight of 132.05 g/mol. Indanone is used as a component of fuels, solvents, and varnishes.

Indanone was found to be important in many applications. In one, indanones were used to synthesize indenopyrazoles[3]. It was found that methyl 3-((6-methoxy-1,4-dihydroindeno[1,2-c]pyrazol-3-yl)amino)-benzoate demonstrated tubulin inhibitor activity toward human cancer cells which showed an antiproliferative effect[3]. This ultimately led to cell growth inhibition. Scheme I shown below how the compound 234 induced arrest in the G_2/M phase in HeLa cells because it inhibited the acetylated tubulin accumulation and microtubule formation. Overall, indanone may serve purposes as a drug candidate for anti-tumor activity[3].



Scheme I: Indanone derived compound 234 has antiproliferative activity

g. Percent Conversion

Percent conversion measures the fraction of the reagent that reacts. In other words, this means the amount of starting material, in this case, indanol, that converted into the product, indanone. This is used to determine the effectiveness of the synthesis reaction. In this experiment, ^{1}H NMR was used to determine percent conversion by tracking proton signals that were present in both indanol and indanone. These signals were then integrated and the values were put into the equation below, with P representing H_A and H_B from indanone and H_A, H_B, H_C, and H_D from indanol.

[(P)/(P+SM)] x 100= percent conversion

h. Factorial Design

Factorial designs have been used in many scientific experiments and research and is a good method to look at how multiple variables can impact synthesis reactions. This method allows for determining the fewest number of experimental runs in order to achieve desired data as well as a way to give as much data as possible for the fewest amount of runs. Factorial design, in this experiment, helps determine the most critical conditions impacting percent conversion[2]. Each variable can be considered separately as well as how they work together to impact results. Factorial design is important to organic synthesis because it can determine the most efficient conditions in a few amount of runs, which may be applied to other synthesis reactions[2].

i. Research Goals

The goal of this research is focused in the microwave irradiation to oxidize indanol to indanone using chromium trioxide resin as the oxidizing agent, while also using a factorial design to determine whether time or temperature have an effect on percent conversion while holding a constant wattage. ^{1}H NMR was used to calculate percent yield of each of the reactions.

After completing the 24 reactions, that Minitab® software generated the parameters for, the next step was to determine which conditions produced the highest

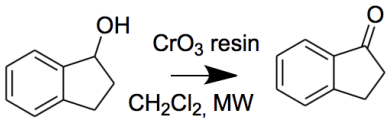
percent yields. ^{1}H NMR of each reaction was run and the percent yield was calculated by tracking protons from the starting material and end product. The data was put into the Minitab® software and a statistical analysis was performed to determine the most efficient conditions. The data from this gives insight to which parameter manipulations were statistically significant and if the two conditions worked synergistically.

The microwave assisted reaction used chromium trioxide resin as the oxidizing agent which also functioned as a catalyst. Time and temperature were increased incrementally from 80 ^{O} C, 100 ^{O} C, and 120 ^{O} C as well as 3 minutes, 5 minutes, 7 minutes, and 10 minutes. Varying these parameters gives insight into the synthesis of indanone from indanol and finding efficient conditions can be beneficial in many regards and industries.

Results and Discussion

a. General Preparation of Indanone
    a. Synthesis

    Indanol was oxidized to indanone by using chromium trioxide resin as the oxidizing agent. Methylene chloride was used as the solvent and these reagents underwent microwave irradiation.



In order to optimize reaction conditions and determine whether the factors of wattage, temperature, and time affected percent conversion, a set of 24 reactions was run using factorial design methodology. The starting material, indanol, was kept constant using a range of .0710 grams to .0750 grams. The amount of the oxidizing agent, chromium trioxide resin, was also kept constant using a range of .6650 grams to .6690 grams. The amount of the solvent, methylene chloride, was kept constant as well at 4 mL. Wattage, temperature, and time were varied. In this particular data set, the wattage used was 600W. The temperature conditions used were 80^{O} C, 100^{O} C, and 120^{O} C. The time conditions were 3 minutes, 5 minutes, 7 minutes, and 10 minutes. Each reaction was run under a specific condition and duplicated. A proton NMR spectrum was taken for each reaction mixture and the results were analyzed by tracking starting material and product protons and translating this data into a percent conversion.

    b. Choice of Reagent

    Chromium trioxide resin was used as the oxidizing agent in all of the reactions. This is due to it being a more environmentally friendly alternative and less toxic than chromium trioxide, its ability to be easily separated from the reaction mixture, and its reusability.

    c. Conditions

    Wattage, temperature, and time were altered to determine which of these factors affected percent yield of each reaction. In this particular data set, the wattage was set to 600W, while time and temperature varied. The temperature conditions included 80^{O} C, 100^{O} C, and 120^{O} C. The time conditions were 3 minutes, 5

minutes, 7 minutes, and 10 minutes. Two factors were kept constant at a time while one was changed. This is so the factor affecting the percent conversion of indanol to indanone could be identified.

d. Percent conversion
The method used to determine how much indanone was produced under microwave irradiation of indanol was percent conversion. In order to calculate this, the ^{1}H NMR spectrum data was analyzed to find protons of indanol, the starting material (SM), and of indanone, the product (P). The integral values of each peak was calculated. To find the percent conversion, the integral values of indanone were divided by the sum of the integral values of both indanone and indanol and then multiplied by 100 to obtain a percentage. The equation can be represented by [(P)/(P+SM)] x 100.

b. Parameter Analysis

a. Percent Conversion as it relates to temperature
With the conditions of 600 watts and 3 minutes, percent yield initially increased from 80^{O} C to 100^{O} C, and then greatly decreased from 100^{O} C to 120^{O} C. From 80^{O} C to 100^{O} C, the percent yield increased 7% from 40% to 47%. From 100^{O} C to 120^{O} C, the percent yield decreased 41% from 47% to 6%.

Table I

Percent Conversion as it Relates to Temperature at 600 watts for 3 minutes.

Wattage	Time (min)	Temperature (°C)	% Conversion Trial I	% Conversion Trial II	Average % Conversion
600	3	80	41.3718723	38.2459611	39.8089167
600	3	100	54.4916508	40.0322191	47.261935
600	3	120	5.29497099	7.42474916	6.35986008

With the conditions of 600 watts and 5 minutes, percent yield also initially increased from 80^{O} C to 100^{O} C, and then decreased from 100^{O} C to 120^{O} C. From 80^{O} C to 100^{O} C, the percent yield increased 19% from 58% to 77%. From 100^{O} C to 120^{O} C, percent yield decreased 11% from 77% to 66%. There is an overall increase of 8% from 80^{O} C to 120^{O} C.

Table II

Percent Conversion as it relates to Temperature at 600 Watts for 5 minutes.

Wattage	Time (min)	Temperature (°C)	% Conversion Trial I	% Conversion Trial II	Average % Conversion
600	5	80	59.4520548	57.5120192	58.482037
600	5	100	79.4124243	75.0886076	77.250516
600	5	120	60.3268945	71.5850736	65.9559841

At the conditions 600 watts and 7 minutes, as the temperature increased, the percent yield also increased. From 80^{O} C to 100^{O} C, the percent yield increased

26% from 41% to 67%. From 100 ^{O}C to 120 ^{O}C, the percent yield increased 25% from 67% to 92%. There is an overall increase of 51% from 80 ^{O}C to 120 ^{O}C.

Table III

Percent Conversion as it relates to Temperature at 600 Watts for 7 minutes.

Wattage	Time (min)	Temperature (°C)	% Conversion Trial I	% Conversion Trial II	Average % Conversion
600	7	80	38.9180672	43.2217279	41.0698976
600	7	100	62.0019675	71.3785047	66.6902361
600	7	120	92.1334923	92.0521339	92.0928131

At the conditions of 600 watts and 10 minutes, as temperature increased, percent yield also increased. From 80 ^{O}C to 100 ^{O}C, the percent yield increased 20% from 48% to 68%. From 100 ^{O}C to 120 ^{O}C, the percent yield increased 19% from 68% to 87%. There is an overall increase of 39% from 80 ^{O}C to 120 ^{O}C.

Table IV

Percent Conversion as it relates to Temperature at 600 Watts for 10 minutes.

Wattage	Time (min)	Temperature (°C)	% Conversion Trial I	% Conversion Trial II	Average % Conversion
600	10	80	53.5516801	43.1502086	48.3509444
600	10	100	62.2096317	73.5362998	67.8729658
600	10	120	87.7934272	86.9384673	87.3659473

Overall, there is a potential trend of increase in percent yield as temperature increases with some outliers.

b. Percent Conversion as it relates to time

At the conditions 600 watts and 80 ^{O}C, no consistent trend was found in the data. From 3 minutes to 5 minutes, there was an increase of 18% in percent yield from 40% to 58%. From 5 minutes to 7 minutes, there was a decrease of 17% in percent yield from 58% to 41%. From 7 minutes to 10 minutes, there was an increase in percent yield of 7%, from 41% to 48%. Overall, from 3 minutes to 10 minutes, there was an increase in percent yield of 8%.

Table V

Percent Conversion as it relates to Time at 600 Watts and 80°C.

Wattage	Time (min)	Temperature (°C)	% Conversion Trial I	% Conversion Trial II	Average % Conversion
600	3	80	41.3718723	38.2459611	39.8089167
600	5	80	59.4520548	57.5120192	58.482037
600	7	80	38.9180672	43.2217279	41.0698976
600	10	80	53.5516801	43.1502086	48.3509444

At the conditions of 600 watts and 100 ^{O}C, a consistent trend was not found. From 3 minutes to 5 minutes, there was a 30% increase in percent yield from 47% to 77%. From 5 minutes to 7 minutes, there was a 10% decrease in percent yield from 77% to 67%. From 7 minutes to 10 minutes, the percent yield increased 1% from 67% to 68%. Overall, there was an increase of 21% in percent yield from 3 minutes to 10 minutes, starting at 47% conversion to 68% conversion.

Table VI

Percent Conversion as it relates to Time at 600 Watts and 100°C.

Wattage	Time (min)	Temperature (°C)	% Conversion Trial I	% Conversion Trial II	Average % Conversion
600	3	100	54.4916508	40.0322191	47.261935
600	5	100	79.4124243	75.0886076	77.250516
600	7	100	62.0019675	71.3785047	66.6902361
600	10	100	62.2096317	73.5362998	67.8729658

At the conditions of 600 watts and 120 ^{O}C, no consistent trend in percent conversion was observed. From 3 minutes to 5 minutes, percent conversion increased 60%, from 6% to 66%. From 5 minutes to 7 minutes, percent conversion increased 26% from 66% to 92%. From 7 minutes to 10 minutes, percent yield decreased 5%, from 92% to 87%. Overall, from 3 minutes to 10 minutes, there was an increase in percent yield of 81%, from 6% to 87%.

Table VII

Percent Conversion as it relates to Time at 600 Watts and 120°C.

Wattage	Time (min)	Temperature (°C)	% Conversion Trial I	% Conversion Trial II	Average % Conversion
600	3	120	5.29497099	7.42474916	6.35986008
600	5	120	60.3268945	71.5850736	65.9559841
600	7	120	92.1334923	92.0521339	92.0928131
600	10	120	87.7934272	86.9384673	87.3659473

Overall, no clear trend was observed in percent conversion as it relates to time, however, in most cases it appears to increase with increasing time.

c. Parameter Analysis Comparison

The overall results show that there may exist a trend in an increasing percent conversion as temperature is increased in the conversion of indanol to indanone. In addition, no sequential trend was found for time as it relates to wattage and temperature.

i. Average Conversion of Indanol to Indanone

The analysis of average percent conversion of indanol to indanone further shows this potential trend of increasing percent yield as temperature increases. It can be noted that the percent conversion range for 80°C was from 39% to 58% with an average percent conversion of 46.5%. It can also be noted that the percent conversion range of 100°C was 47% to 68% with an average percent conversion of 64.75%. In addition, the percent

conversion range of 120°C, excluding the extreme outlier, was 66% to 92% with an average percent conversion of 81.83%. This trend indicates that increasing temperature may increase percent conversion.

Table VIII

Average Conversion of Indanol to Indanone

Wattage	Time (min)	Temperature (°C)	% Conversion Trial I	% Conversion Trial II	Average % Conversion
600 W	3	80°C	41%	38%	39%
600 W	5	80°C	59%	57%	58%
600 W	7	80°C	39%	43%	41%
600 W	10	80°C	54%	43%	48%
600 W	3	100°C	54%	40%	47%
600 W	5	100°C	75%	79%	77%
600 W	7	100°C	62%	71%	67%
600 W	10	100°C	62%	74%	68%
600 W	3	120°C	5%	7%	6%
600 W	5	120°C	60%	72%	66%
600 W	7	120°C	92%	92%	92%
600 W	10	120°C	88%	87%	87.5%

Overall, through comparison of how altering temperature and time affected percent conversion, it appears that only temperature had a possible effect on the amount of indanol converted to indanone through microwave irradiation.

c. H1 NMR and Spectral Analysis of Indanone

a. Identification of Protons used to Calculate Percent Conversion

^{1}H FT-NMR spectra was taken of pure indanol and indanone to determine protons to analyze when calculating percent conversion. The indanol protons, H_A (3.0-3.1), H_B (2.7-2.9), H_C (2.4-2.6), and H_D (1.8-2.0) and the indanone protons, H_A (3.1-3.2) and H_B (2.6-2.8) were chosen because these protons are present in both starting material and product but have different chemical shifts in their respective spectra (Figure 1). The integral values of each set of protons was used to calculate the percent conversion (Table).

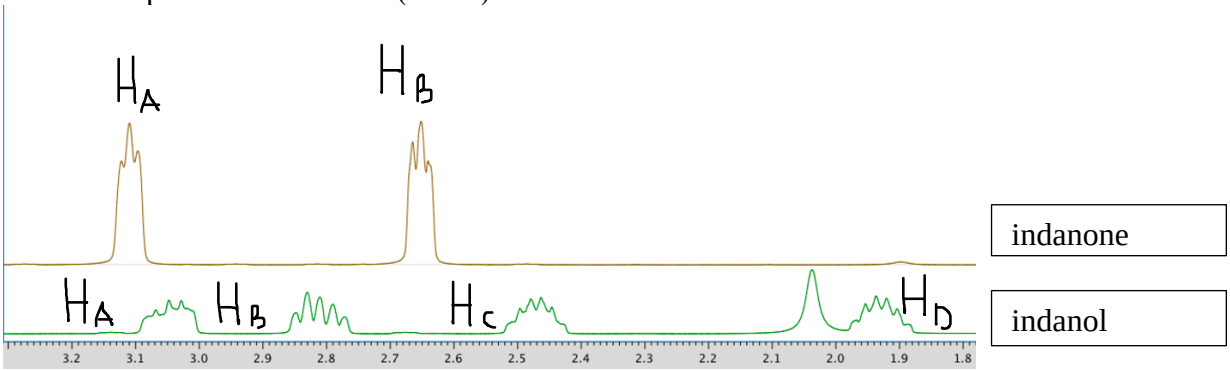


Figure 1: ^{1}H-NMR Spectra (400 MHz, $CDCl_3$) of Pure Indanol and Pure Indanone

Table IX

Chemical Shifts (400MHz, ppm) of Protons in Indanol and Indanone

Proton at Position	Indanol	Indanone
H_A	δ3.0-3.1	δ3.1-3.2
H_B	δ2.7-2.9	δ2.6-2.8
H_C	δ2.4-2.6	
H_D	δ1.8-2.0	

b. Calculation of Percent Conversion of Indanone
The percent conversion of indanone was calculated by dividing the integral values of indanone, H_A and H_B, corresponding to the product (P) by the sum of the integral values of both the starting material, indanol (SM) and product (P), indanone. This was then multiplied by 100. Percent conversion can be represented by the equation [(P)/(P+SM)] x 100= percent conversion.

c. H1 NMR Spectral Analysis of Oxidation of Indanol to Indanone at constant wattage, time, and varying temperature.
^{1}H NMR was used to determine the effect of temperature on percent yield of indanol to indanone at a constant time and wattage. The temperature conditions used were 80°C, 100°C, and 120°C. Percent yield was calculated by comparing the H_A and H_B integrals (δ2.8-3.1) in indanone to the H_A, H_B, H_C, H_D (δ1.8-3.0) integrals in indanol.

At 600 watts for 3 minutes, the temperature conditions varied from 80°C which had a percent conversion of 40%, 100°C which had a percent conversion of 47%, and 120°C which had a percent conversion of 6%. The percent conversion increased from 80°C to 100°C.

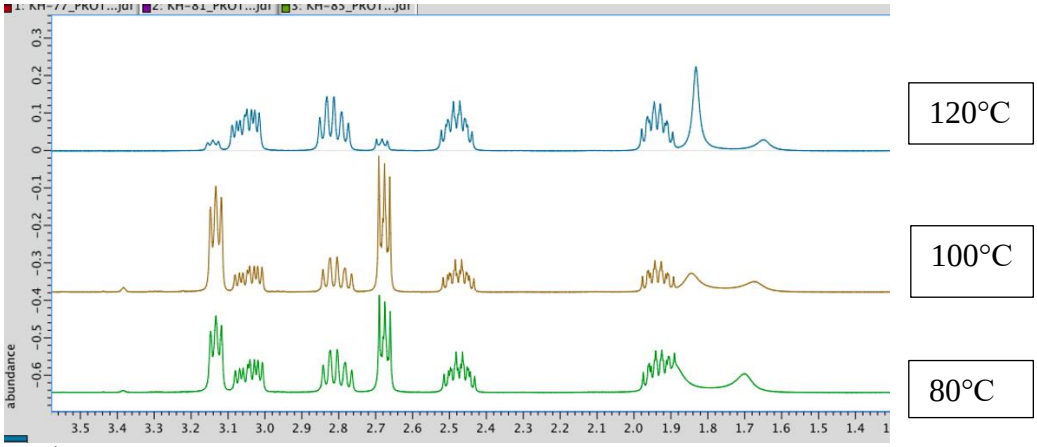


Figure II: ^{1}H-NMR Spectra (400MHz, $CDCl_3$) of the conversion of indanol to indanone at 600 watts, three minutes, and 80°C, 100°C, and 120°C.

Table X

Integral height of indanol and indanone percent conversion to indanone at 80°C, 100°C, and 120°C, 600 watts, and three minutes

Temperature (°C)	Indanol H_A	Indanol H_B	Indanol H_C	Indanol H_D	Indanone H_A	Indanone H_B	Percent Conversion Indanone
80	6.47	7.34	7.26	6.11	9.61	9.57	40%
100	2.85	3.22	3.18	5.64	4.88	5.06	47%
120	3.66	3.91	4.02	2.25	.56	.55	6%

At 600 watts for 5 minutes, the temperature conditions varied from 80°C which had a percent conversion of 58%, 100°C which had a percent conversion of 77%, and 120°C which had a percent conversion of 66%. The percent conversion increased from 80°C to 100°C.

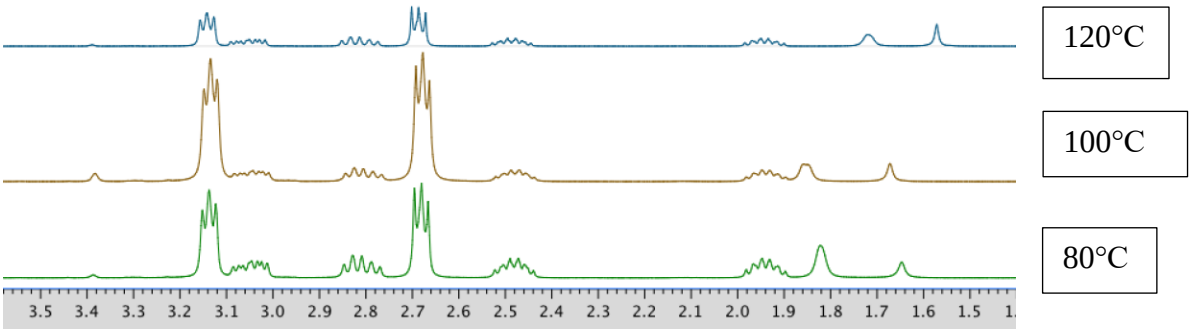


Figure III: ^{1}H-NMR Spectra (400MHz, $CDCl_3$) of the conversion of indanol to indanone at 600 watts, five minutes, and 80°C, 100°C, and 120°C.

Table XI

Integral height of indanol and indanone percent conversion to indanone at 80°C, 100°C, and 120°C, 600 watts, and five minutes

Temperature (°C)	Indanol H_A	Indanol H_B	Indanol H_C	Indanol H_D	Indanone H_A	Indanone H_B	Percent Conversion Indanone
80	3.78	4.24	4.05	4.21	11.79	12.08	58%
100	1.80	2.58	2.50	2.30	17.71	17.70	77%
120	1.31	1.17	1.38	1.48	4.10	4.02	66%

At 600 watts for 7 minutes, the temperature conditions varied from 80°C which had a percent conversion of 41%, 100°C which had a percent conversion of 67%, and 120°C which had a percent conversion of 92%. The percent conversion increased from 80°C to 120°C.

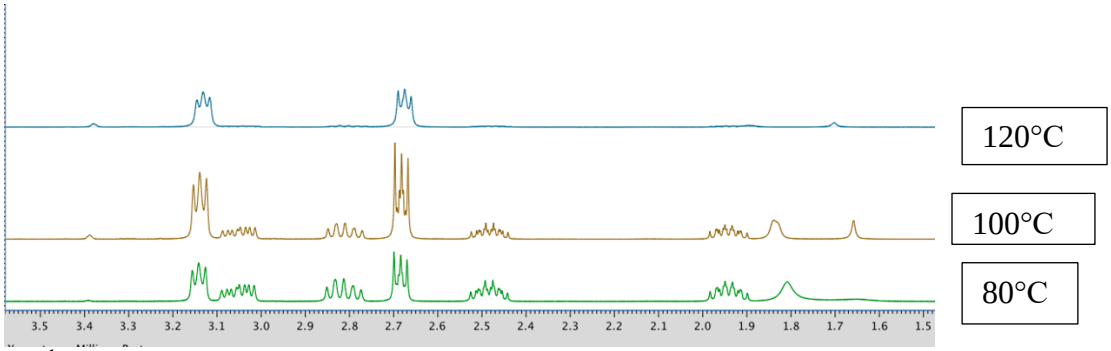


Figure IV: ^{1}H-NMR Spectra (400MHz, $CDCl_3$) of the conversion of indanol to indanone at 600 watts, seven minutes, and 80°C, 100°C, and 120°C.

Table XII

Integral height of indanol and indanone percent conversion to indanone at 80°C, 100°C, and 120°C, 600 watts, and seven minutes

Temperature (°C)	Indanol H_A	Indanol H_B	Indanol H_C	Indanol H_D	Indanone H_A	Indanone H_B	Percent Conversion Indanone
80	5.75	5.64	5.97	5.90	7.47	7.35	41%
100	3.65	3.91	3.95	3.94	12.69	12.52	67%
120	.14	.36	.29	.53	7.83	7.63	92%

At 600 watts for 10 minutes, the temperature conditions varied from 80°C which had a percent conversion of 48%, 100°C which had a percent conversion of 68%, and 120°C which had a percent conversion of 87%. The percent conversion increased from 80°C to 120°C.

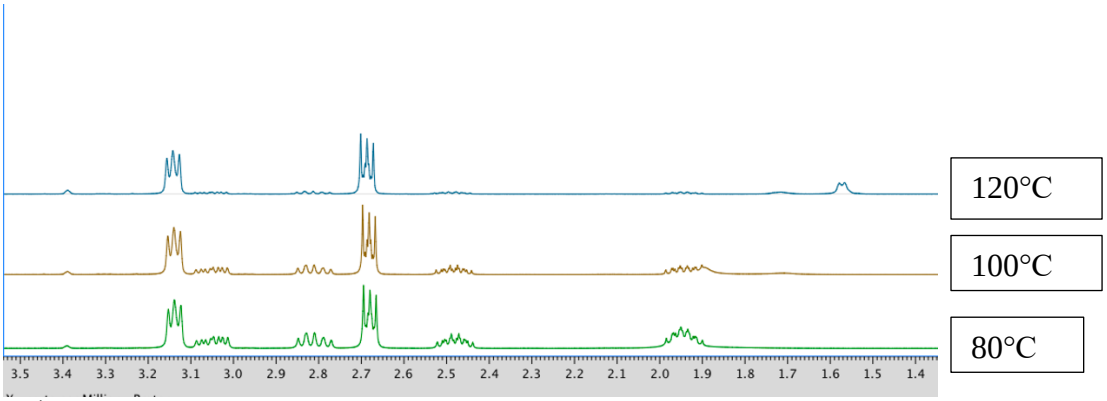


Figure V: ^{1}H-NMR Spectra (400MHz, $CDCl_3$) of the conversion of indanol to indanone at 600 watts, ten minutes, and 80°C, 100°C, and 120°C.

Table XIII

Integral height of indanol and indanone percent conversion to indanone at 80°C, 100°C, and 120°C, 600 watts, and ten minutes

Temperature (°C)	Indanol H_A	Indanol H_B	Indanol H_C	Indanol H_D	Indanone H_A	Indanone H_B	Percent Conversion Indanone
80	2.50	2.57	2.53	3.32	6.39	6.20	48%
100	1.01	1.62	1.55	2.49	4.85	6.13	68%
120	.39	.39	.40	.38	5.61	5.61	87%

d. H1 NMR Spectral Analysis of Oxidation of Indanol to Indanone at constant wattage, temperature, and varying time.
^{1}H NMR was used to determine the effect of time on percent yield of indanol to indanone. The durations of time used were three minutes, five minutes, seven minutes, and ten minutes. Percent yield was calculated by comparing the H_A and H_B integrals (δ2.8-3.1) in indanone to the H_A, H_B, H_C, H_D (δ1.8-3.0) integrals in indanol.

At 600 watts for 80 degrees Celcius, the time varied from three minutes, which had a percent conversion of 40%, five minutes which had a percent conversion of 58%, seven minutes which had a percent conversion of 41%, and ten minutes which had a percent conversion of 48%. The percent conversion increased overall as time increased.

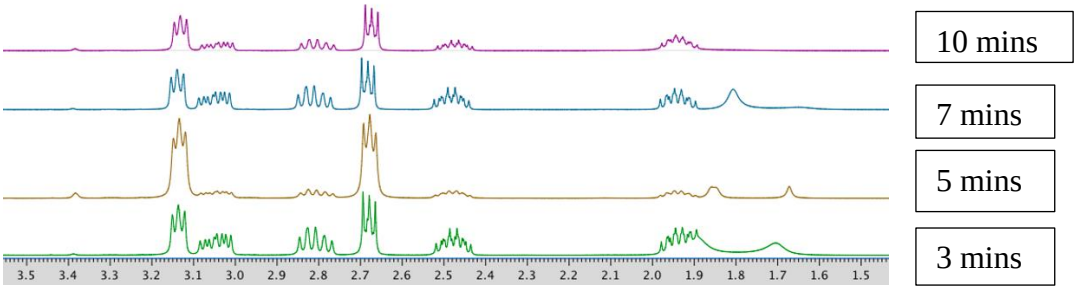


Figure VI: ^{1}H-NMR Spectra (400MHz, $CDCl_3$) of the conversion of indanol to indanone at 600 watts, 80°C, and 3 minutes, 5 minutes, 7 minutes, and 10 minutes.

Table XIV

Integral height of indanol and indanone percent conversion to indanone at 3 minutes, 5 minutes, 7 minutes, and 10 minutes at 600 watts, and 80 degrees Celcius

Time (minutes)	Indanol H_A	Indanol H_B	Indanol H_C	Indanol H_D	Indanone H_A	Indanone H_B	Percent Conversion Indanone
3	6.47	7.34	7.26	6.11	9.61	9.57	40%
5	1.14	1.54	1.56	2.83	4.82	5.15	58%

7	5.75	5.64	5.97	5.90	7.47	7.35	41%
10 113	2.50	2.57	2.53	3.32	6.39	6.20	48%

At 600 watts for 100 degrees Celcius, the time varied from three minutes, which had a percent conversion of 47%, five minutes which had a percent conversion of 77%, seven minutes which had a percent conversion of 67%, and ten minutes which had a percent conversion of 68%. Overall, the percent conversion increased as time increased.

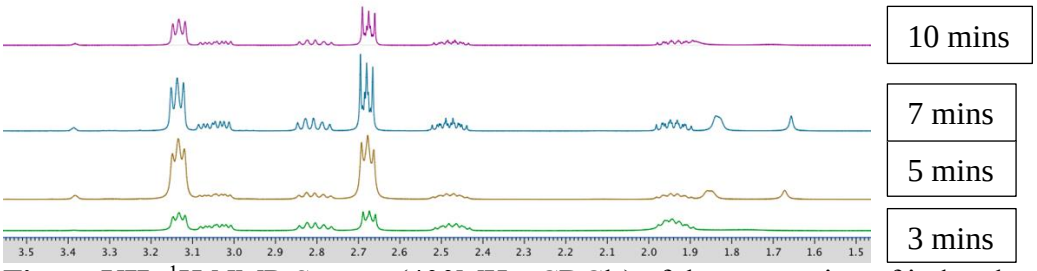


Figure VII: ^{1}H-NMR Spectra (400MHz, $CDCl_3$) of the conversion of indanol to indanone at 600 watts, 100°C, and 3 minutes, 5 minutes, 7 minutes, and 10 minutes.

Table XV

Integral height of indanol and indanone percent conversion to indanone at 3 minutes, 5 minutes, 7 minutes, and 10 minutes at 600 watts, and 100 degrees Celcius

Time (minutes)	Indanol H_A	Indanol H_B	Indanol H_C	Indanol H_D	Indanone H_A	Indanone H_B	Percent Conversion Indanone
3	2.85	3.22	3.18	5.64	4.88	5.06	47%
5	1.80	2.58	2.50	2.30	17.71	17.70	77%
7	3.65	3.91	3.95	3.94	12.69	12.52	67%
10 117	1.01	1.62	1.55	2.49	4.85	6.13	68%

At 600 watts for 120 degrees Celcius, the time varied from three minutes, which had a percent conversion of 6%, five minutes which had a percent conversion of 66%, seven minutes which had a percent conversion of 92%, and ten minutes which had a percent conversion of 87%. Overall, an increase in percent conversion with an increase of time was noted.

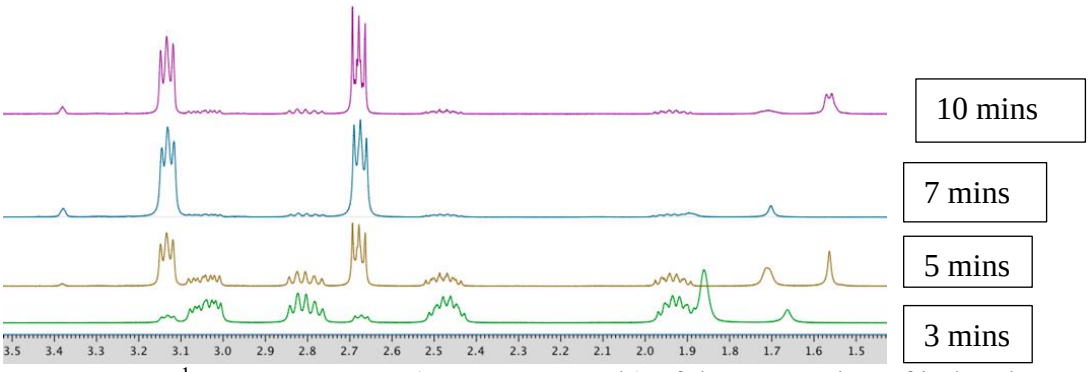


Figure VIII: ^{1}H-NMR Spectra (400MHz, $CDCl_3$) of the conversion of indanol to indanone at 600 watts, 120°C, and 3 minutes, 5 minutes, 7 minutes, and 10 minutes.

Table XVI

Integral height of indanol and indanone percent conversion to indanone at 3 minutes, 5 minutes, 7 minutes, and 10 minutes at 600 watts, and 120 degrees Celcius

Time (minutes)	Indanol H_A	Indanol H_B	Indanol H_C	Indanol H_D	Indanone H_A	Indanone H_B	Percent Conversion Indanone
3	3.66	3.91	4.02	2.25	.56	.55	6%
5	1.31	1.17	1.38	1.48	4.10	4.02	66%
7	.14	.36	.29	.53	7.83	7.63	92%
10 121	.39	.39	.40	.38	5.61	5.61	87%

Factorial Design Analysis

The MiniTab software was used to analyze percent conversion collected from the ^{1}HMR data. The reaction parameters used in the factorial design are listed in Appendix I. The analysis of the percent conversion of the reaction of indanol to indanone by Minitab included model summary statistics, p-values, a Pareto chart, and residual plots. Each of these representations of the data help determine if the factorial design model used fits the data collected of the microwave oxidation of indanol to indanone.

1. Pareto Chart of the Standardized Effects of Time and Temperature
   Pareto charts indicates the frequency of defects in addition to their cumulative impact. This pareto chart compare the relative magnitude and statistical significance of the data collected with varying parameters. The chart shows an error term of 2.18 which shows the absolute value of the standardized effects from largest effect to smallest effect. According to Figure 2, time had the greatest impact on percent conversion because this bar extends the furthest. Also according to Figure 2, temperature had the least impact on percent conversion because it extends the least across the chart. Figure 2 also demonstrates that the combination of time and temperature had the second greatest

impact on percent conversion of indanol to indanone due to it being the second furthest extending bar across the chart. Pareto charts allow for a visual representation on which parameters impacted percent conversion of indanol to indanone the most.

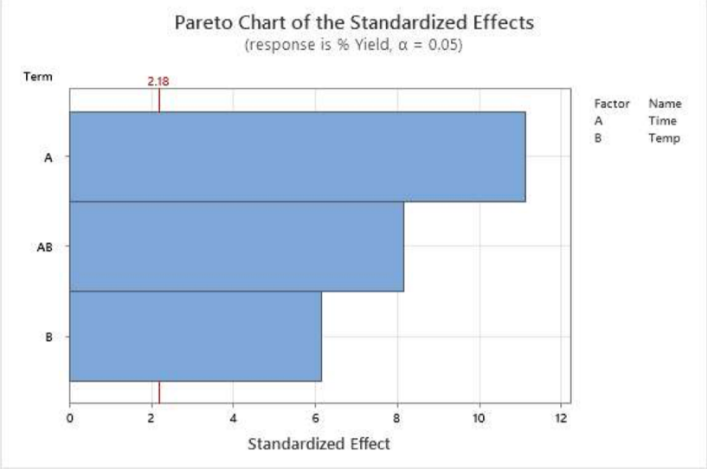


Figure II: Pareto Chart of Standardized Effects for parameters of time and temperature demonstrates effects of these parameters on percent conversion of indanol to indanone.

2. Statistic Significance of Time and Temperature

The p-value of a data set allows one to determine which factors are statistically significant. The significance level (α) is equal to 0.05 and this is what is compared to the p-value associated with the data collected. The significance level determines the amount of risk associated with determining a variable and an effect have a relationship. A p-value of 0.05 or less mean that the data is significant.

The data showed that both time and temperature as well as the two-way interactions of these variables had a p-value of 0.000. This means that time as well as temperature and the two variables working together will impact the results of percent conversion. More data points added to this factorial model will help distinguish these results more. With the data points collected from the experiments, an increase in temperature and time, as well as an increase in both time and temperature will likely lead to an increase in percent conversion.

Analysis of Variance

Source	DF	Adj SS	Adj MS	F-Value	P-Value
Model	11	12339.8	1121.80	36.58	0.000
Linear	5	7501.1	1500.22	48.92	0.000
Time	3	5947.5	1982.50	64.65	0.000
Temp	2	1553.6	776.79	25.33	0.000
2-Way Interactions	6	4838.8	806.46	26.30	0.000
Time*Temp	6	4838.8	806.46	26.30	0.000
Error	12	368.0	30.67		
Total	23	12707.8			

Figure III: P-value as it relates to temperature and time

3. Model Summary
   Model summaries determine how well the model fits the data collected (Table 17). S-values determine how well the model defines the result. The R-squared value also determines how well the data fits. In this model, the R-squared value was 97.10. The closer the value is to 100, the better the data fits the model. The adjusted R-sq value for the data collected is high at 94.45% meaning that the data also fits the model well with a predictor added. The predicted R-squared value was also high from this data, at 88.42%, indicating the data set has strong predictability. These values can be used to determine which model best suits a set of data.

Table 17

Model Summary for the data of the conversion of indanol to indanone under various microwave parameters.

S	R-sq	R-sq (adj.)	R-sq (pred.)
5.53775	97.10	94.45%	88.42%

4. Residual Plots
   Residual plots are also a source to determine how well the data fits the model. Figure IV indicates a normal residual plot, residual versus fitted value plot, residual versus frequency histogram, and observation order versus residual plot. The normal probability plot should follow a straight line in order to allow for the verification of the assumption that the residuals are distributed normally. In the plot made from the data, it is shown that the points follow a straight line and may be considered normal. The residual versus fitted value plot will show the assumption that residuals are randomly distributed and have a constant variance if the plots are distributed randomly. The plot made from the data show that the points fall on both sides of the line in no true specific pattern. The residual versus observation order chart should indicate that the residuals are independent from one another. The data showed points that fall in a random pattern around the center line of the

plot, meaning that the residuals are in fact independent from each other. The histogram should depict a bell-shaped curve in order to indicate that the model fits the data. From the data collected, the histogram almost takes a bell shape, indicating that the model fits the data.

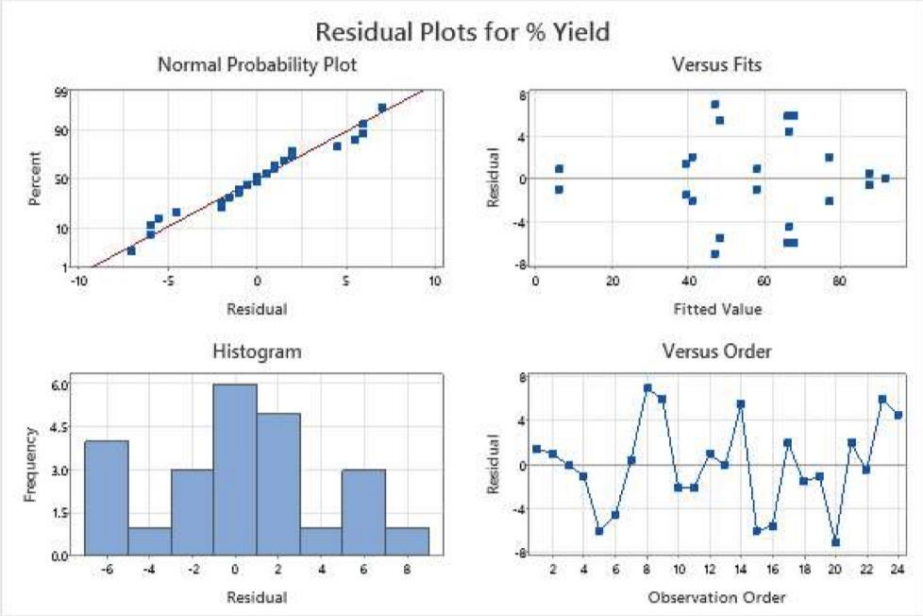


Figure IV: Residual Plots from the data set of the conversion of indanol to indanone.

5. Factorial Design Conclusion
   The results collected from the MiniTab factorial design software indicate that the factors of time and temperature have statistically significant effects on percent conversion. Each component of the data analysis, such as the Pareto chart of effects, p-values, model summary statistics, and residual plots help verify that the data collected from the microwave and ^{1}H-NMR fit the model used on MiniTab software. The R-squared value of 97% show that the individual and interacting parameters, such as time and temperature, have an effect on percent conversion of indanol to indanone. The data also shows that time and temperature parameters are significant because as these values increase, the percent yield also tended to increase. The data collected from MiniTab further supports the conclusion that temperature, time, and the interaction of these two variables affect percent conversion of indanol to indanone.

Overall Comparison

Indanone was synthesized by the oxidation of Indanol using chromium trioxide resin as the oxidation agent and dichloromethane as a solvent. The reaction was heated under microwave irradiation where wattage was held constant but temperature and time were varied. The condition of 600 watts, 120 degrees Celcius, and 7 minutes gave the highest percent yield an average of 92% between the two trials.

From analyzing the individual parameters, it was shown that both temperature and time have an effect on percent conversion, with increasing time and temperature correlating with

increasing percent yields. Factorial analysis also supports this finding, as it was indicated that both had an effect on overall percent yield.

Future Work

Future of oxidizing secondary alcohols can be done to determine which parameters more significantly impact percent conversion or determining other parameters that have an effect on percent conversion other than temperature and time. Future work on the effect of altering wattage in the microwave should also be done to see if there are any trends that indicate impact on percent yield.

Experimental

Each of the microwave reactions were performed in a multimode Milestone StartSYNTH microwave oven in a multimode cavity [37 x 34.5 x 33.5 (h) cm] with a rotation system. The reaction parameters such as wattage, time, and temperature, were adjusted and controlled by the ™™StartSYNTH terminal controller. Inside the microwave, a ATC-FO sensor was used inside the reaction vessel and an external IRTC sensor in the microwave cavity were used to monitor temperature.

The following was purchased from Sigma-Aldrich Company: indanol, polymer-supported chromic acid resin on Amberlyst ® A-26 (microporous, 20-50 mesh, extent of labeling: ~2.5 mmol/g loading), and chloroform-*d* [99.8 atom % D, containing 0.1% (v/v) TMS]. From Fishcer Scientific Company, dichloromethane (submicron filtered) was purchased.

General Procedure

Each reaction was run in a 25 mL quartz closed-pressurized reaction vessel with a magnetic stir bar and Weflon ™ bar. 0.710-0.750 grams of indanol (5.4×10^{-4} mols) was dissolved in 4 mL of dichlormethane. Polymer-supported chromic acid, .6650-.6690 grams (5.4×10^{-4} mols) was added and then the reaction vessel was placed in the StartSYNTH laboratory microwave oven and irradiated at 600 watts with varying temperature and time.

The resulting reaction mixture was filtered using filter paper and a funnel and the resin was collected in a 25 mL round bottom flask. The resin was washed three times with dichloromethane. The rotary evaporator was used to remove the dichloromethane from the reaction mixture. The remaining mixture was analyzed using ^{1}H NMR run in deuterated chloroform.

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