RESEARCH ARTICLE

Open Access

Progress towards a more sustainable synthetic pathway to ibuprofen through the use of solar heating

Brian M. Agee, Gene Mullins and Daniel J. Swartling*

Abstract

The ACS Green Chemistry Institute Pharmaceutical Roundtable was formed in 2005 to encourage the incorporation of green chemistry techniques into the synthetic pathways of pharmaceuticals. Through this initiative, synthetic pathways of several pharmaceuticals have been altered to adapt more environmentally friendly procedures. The amount of electricity required to complete chemical reactions have become an environmental concern due to depleting fossil fuels. A technique was recently developed in which satellite dishes were repurposed as solar reflectors capable of providing a heat source through solar irradiation. The ability to use the solar reflector as the sole heat source for synthetic reactions has been analyzed for the commercially important pharmaceutical, ibuprofen. Ibuprofen synthesis also incorporates chemicals that are not particularly friendly to the environment. The exchange of these chemicals with more environmentally friendly substitutes has been analyzed. The goal of this study is to incorporate a solar energy heat source to develop an alternative energy, more environmentally friendly pathway to ibuprofen.

Keywords: Solar organic synthesis, Solar reflector, Ibuprofen synthesis, Green chemistry, Reactions and methods

Background

Ibuprofen is a nonsteroidal anti-inflammatory drug that is commonly used worldwide for pain relief and fever/inflammation reduction [1]. It was discovered in the 1960s by Andrew Dunlop, who initially tested the drug on cures for hangovers. The drug was first made available via prescription in 1974 (United States) and soon became available as an over the counter drug purchasable at retail shops around the globe [2].

The synthetic procedure to synthesize ibuprofen was patented by the Boots Pure Drug Company in the 1960s (Fig. 1). Their synthetic process involved several complicated steps that generated a considerable amount of chemical waste [3]. Since the Boots method of synthesizing ibuprofen generated an enormous amount of waste when performed on the industry scale, alternative synthetic routes the drug have became of public interest.

In 1992, BHC Company unveiled a new, alternative process of synthesizing ibuprofen (Fig. 2) that was much more environmentally friendly and a model of "atom economy" [4]. This procedure is now owned by BASF and is used as the synthetic procedure for the production of this pharmaceutical. The plant generates approximately 7.7 million pounds of ibuprofen per year representing about 20–25 % of the global production of this pharmaceutical [5].

Electricity is needed for most synthetic steps in both the BHC and Boots method of synthesizing ibuprofen. Most of the electricity in the United States is generated from fossil fuels, thus the usage of electricity has some form of environmental impact associated with it. Solar and water-based energy generation processes, which are virtually greenhouse gas emission-free, have been engineered and implemented in various parts of the United States [6]. The solar oven was recently introduced a possible heat source for chemical reactions [7]. However, it has been determined that solar ovens have the capacity to only heat up to approximately 170 °C, far less than some known synthetic reactions [8].

*Correspondence: dswart@tntech.edu Department of Chemistry, Tennessee Technological University, Cookeville, TN 38505, USA



Recently, it was shown that solar energy could be used to perform high temperature chemical reaction as the heat source [9-12]. A solar reflector was designed out of satellite dishes and Mylar[®] tape, and a Friedel–Crafts acylation reaction was performed using the solar reflector as the sole thermal heat source.

The goal of this study was to synthesize ibuprofen without the use of any fossil fuels for electricity. This particular reaction was chosen based on its current synthetic processes in industry and because advancements in the reaction are currently needed in order to incorporate more sustainable and environmentally friendly techniques. Not only did we intend to modify the synthetic

procedure for ibuprofen by using only solar energy as the heat source, but we intended to modify and develop new synthetic techniques that incorporate the use of more environmentally friendly and sustainable chemical reagents to synthetic pathway of ibuprofen. It is hoped, as a result of this work that a synthesis of ibuprofen can be taught in teaching labs as a "green synthesis" experiment or potentially scaled up to fit the needs of industry.

Results and discussion

A solar reflector was designed through the repurposing of satellite dishes into a reflective parabolic mirror to serve as the sole heat source for synthetic chemical

reactions [9]. The surface of the satellite dish was completely covered with Mylar[®] tape to give it reflective properties capable of generating heat when directed at the sun. The feed horn of the satellite dish was removed and reaction flasks were placed in this position in order to achieve maximum intensity from the directed sunlight.

This work demonstrated that the modified solar heat source can be used successfully in the place of an electric heating source. The solar heat source was able to synthesize a commercially important pharmaceutical product from a well-known, high temperature reaction. Furthermore, the solar heat source was observed to be capable of generating reaction yields that were comparable to the same scale reaction performed using an electric heat source. Also seasonal variations do not seem to cause reaction problems as long as sunlight is present. Furthermore, the intensity of the light did not seem to produce any major problems either. As long as the solar irradiation levels were 500 W/m² or greater, the location, time and day did not seem to affect the results of the solar reactions. Similar results for reactions were obtained during all seasonal periods throughout various times of the day [9-12].

By exposing the round bottom flasks to direct contact with the focal point, a very efficient heating method to provide thermal energy to a chemical reaction without using electricity was established. Through the use of the solar reflector heat source, no electrical waste is being generated since the only energy being used is the energy from the sun, which is renewable.

A Fisher Scientific thermocouple (with a temperature range of $-200\,^{\circ}\text{C}$ to $+1370\,^{\circ}\text{C}$) was used to monitor the reflux temperatures. Reaction temperatures were controlled simply by proportioning the solar reflector in order to allow more or less of the focal point to be directed at the center of the flask. If more heat was needed in order to raise the temperature reaction, the focal point should be completely directed at the center of the flask. If a lower, more controlled temperature is desired, the focal point needs to be held slightly off-center, which allows the researcher to easily control the temperature of the reaction through careful monitoring.

The process described in this manuscript also details a method of producing ibuprofen in a much more environmentally friendly manner. All reactions were carried out under air environment conditions and therefore oxygen does not appear to play any role in the reaction process, with the exception of the Grignard reaction. The Grignard reaction is a moisture sensitive reaction, and thus a drying apparatus had to be applied to the set-up to successfully carry out this reaction. We have exchanged non-environmentally friendly chemicals with substitutes that are often bio-degradable, synthesized from renewable feedstocks, and are less hazardous to our environment. Chemicals for this project were purchased from Acros Organics, Sigma-Aldrich Chemical Company, Alfa

Table 1 Chemical reagents list

Chemical	Company	CAS#
Benzene	Fischer scientific	71-43-2
Isobutyryl chloride	ACROS organics	79-30-1
Aluminum chloride	ACROS organics	7446-70-0
Hydrazine hydrate	Sigma alderich	10217-52-4
Propylene glycol	ACROS organics	57-55-6
Ethylene glycol	ACROS organics	107-21-1
Diethylene glycol	ACROS organics	111-46-6
Glycerol	ACROS organics	56-81-5
Potassium hydroxide	Fischer scientific	1310-58-3
Acetyl chloride	ACROS organics	75-36-5
Sodium borohydride	ACROS organics	16940-66-2
Hydrochloric acid	Fischer scientific	7647-01-0
Methanol	Fischer scientific	67-56-1
Petroleum ether (30-60)	Fischer scientific	68476-82-6
Sodium sulfate	Fischer scientific	7757-82-6
Tetrahydrofuran	Sigma alderich	109-99-9
Magnesium	Fischer scientific	7439-95-4
1,2-dibromoethane	Eastman organic chemicals	106-93-4
Carbon dioxide	Air gas USA	124-38-9
Diethyl ether	Fischer scientific	60-29-7
Sodium hydroxide	Fischer scientific	1310-73-2
Anthracene	Fischer scientific	120-12-7
Maleic anhydride	Fischer scientific	108-31-6
Toluene	Fischer scientific	108-88-3
Calcium Chloride	Fischer scientific	10043-52-4

Aesar, and TCI America. All reagents and solvents used in the research were used without further purification. Table 1 provides a detailed list of all reagents used during the research process. Furthermore, we have developed a method of synthesizing this compound with the use of fossil fuel derived electricity. The incorporation of a solar energy heat source and use of environmentally friendly chemicals has provided a new synthetic pathway to ibuprofen that can be taught in teaching labs as a "green synthesis" experiment or scaled to fit the needs of industrial synthesis.

As seen in Table 2, a new synthetic route to ibuprofen has been developed in which each step in the synthetic pathway uses no fossil fuel derived electrical energy. Furthermore, each step in the synthetic pathway has a comparable product yield (within experimental error) when comparing the solar heated procedure to the electrical heated procedure. The only step that appears to have a yield difference not within experimental error is the reaction to synthesize isobutyrophenone. Since the temperatures and reaction times were identical, it can only be assumed that some other factor played a role in the yield difference.

Table 2 Comparison of solar vs. electric technique for complete synthesis of ibuprofen

Compound	Technique	% Yield
Isobutyrophenone	In lab	55
	Solar	83
Isobutylbenzene	In lab	67
	Solar	62
4'-isobutylacetophenone	In lab	51
	Solar	60
1-chloro-1-(4-isobutyphenyl)ethane ibuprofen	In lab	88
	In lab	33
	Solar	27

Through the use of a P4400 Kill A Watt® power meter [13], it was determined that the amount of energy in kilowatt-hours (KWH) for the total synthesis and purification of ibuprofen using this synthetic technique required approximately 4.0 kWh. Since no electricity is consumed when using solar energy as the thermal heat source, the only electrical requirements for this process would be that from the purification step (0.13 kWh for vacuum distillation). Thus, using the current step-up as proposed, approximately 3.5 kWh of energy is saved for the entire synthesis of ibuprofen. This result would be observed on both small scale reactions as reported or for industrial scale reactions. The only difference when comparing the small scale reactions to industry scale reactions is that the KWH for the synthetic and purification steps would scale due to the larger volume. However, by using the solar reflector thermal heat source, all electricity usage for the synthetic process would be removed, and the only energy consumption would come from the purification process.

Safety concerns arose concerning reactions being performed at elevated temperatures outside of the confines of a chemical fume hood. Since the chemical reactions are being performed outside, the fumes generated during the reactions escaped into the environment just as they would if the reaction was performed inside a fume hood. In the case of using the solar reflector as a heat source, the outside environment acts as a "natural" fume hood to disperse the fumes. As long as the researchers are not constantly standing directly over the openings of the reaction, expose to fume levels are no more than students working on a bench top in an undergraduate chemical laboratory.

Experimental

Development of the solar heat source

The same design for the solar reflector was used as the reflector in our previous publications [9-11]. The solar



Fig. 3 Solar reflector design. A solar reflector was designed through the repurposing of an unused satellite dishes into a reflective parabolic mirror that will serve as the sole heat source to drive synthetic chemical reactions to completion. Satellite dishes were completely covered with Metalized Mylar[®] tape to attain the reflective properties needed to generate heat

reflector was developed through the repurposing of a satellite dish into a reflective parabolic mirror (Fig. 3). The satellite dish was completely covered with metalized Mylar[®] tape to attain the reflective properties needed to generate heat. Since the feed horn of the dish is located at the focal point, it was removed and reaction flasks were placed in this position in order to achieve maximum intensity from the sunlight. Round bottom flasks that were used as the reaction vessels were painted black up to approximately half-way up the flask using VHT® Flame Proof paint, which can withstand intermittent temperatures up to 1093 °C. The round bottom flasks were painted to prevent photochemical side reactions and allow for an efficient heating process. The synthesis consists of five steps, beginning with the Friedel-Crafts acylation of benzene (Fig. 4).

Isobutyrophenone synthesis

The synthetic procedure for this step has been published in a previous manuscript [9]. Benzene underwent a Friedel–Crafts acylation with isobutyryl chloride to synthesize isobutyrophenone. The reaction was performed using excess benzene as a replacement for a typical solvent and heat to reflux (88 °C) for a period of 3 hours. Any unreacted benzene was recovered after the reaction during the distillation process. A 66 % yield of isobutyrophenone was obtained from the solar synthesis, compared to a 44 % yield from an in-lab, electrical heating analysis.

Isobutylbenzene synthesis

The synthetic procedure for this step has been published in a previous manuscript [10, 11]. Isobutyrophenone, from the previous reaction, underwent a Wolff–Kishner reduction using hydrazine hydrate and strong base conditions to synthesize isobutyl benzene. The solvent for this reaction was replaced with the more sustainable solvent glycerol. The glycerol for this reaction was obtained from the synthesis of biodiesel. The reaction was allowed to heat at reflux (149–155 °C) for a period of three hours. An average 51 % yield of isobutyl benzene was obtained from the solar synthesis, compared to a 55 % yield from an in-lab, electrical heating analysis.

Isobutylacetophenone synthesis

A solution of isobutyl benzene (61.4 mmol), acetyl chloride (57.3 mmol), and aluminum chloride (25.1 mmol) was placed into a 25 mL round bottom flask. The flask was then placed in an aluminum heating block that was attached to the solar heat source near the point at which the focal point was going to be located. Because the reaction was required to reflux for a certain amount of time, a condenser was filled with cold water and capped with pipet bulbs to ensure that the water stayed in the condenser (Fig. 5). The same procedure as used in the synthesis of isobutyrophenone was incorporated into this synthetic procedure. The solar heat source was then moved into a position in which it was reflecting sunlight such that the focal point of the sunlight was directed at the bottom of the aluminum block. The solution was allowed to reflux at a temperature of 49-58 °C for a period of three hours. After reflux period was complete, the solution was washed with methanol and poured over ice. The product was extracted using dichloromethane and dried over calcium chloride. Pure isobutylacetophenone was obtained via vacuum distillation. The in-lab study of this chemical reaction was conducted using the same molar amounts of each reactant, but the reaction was heated using a Fisher Scientific hotplate.

A 60 % yield (6.015 g) of isobutylacetophenone was obtained when the Friedel–Crafts acylation of benzene was performed with the solar reflector, while a comparative study using an electric heat source only had a 51 % yield (5.113 g) of isobutylacetophenone. Spectral analysis using 1H and ^{13}C NMR identified the products. 1H NMR (300 MHz, CDCl₃): $\delta7.893$ (2H, m, J = 5.4 Hz), $\delta7.313$ (2H, m, J = 5.8 Hz), $\delta2.581$ (3H, s, J = 2.1 Hz), $\delta2.522$ (2H, t, J = 5.4 Hz), $\delta1.874$ (1H, m, J = 5.1 Hz, 10.2 Hz), $\delta0.913$ (6H, q, J = 4.5 Hz). ^{13}C NMR (300 MHz, CDCl₃): $\delta197.002$, $\delta146.36$, $\delta135.169$, $\delta129.509$, $\delta128.224$, $\delta45.227$, $\delta30.76$, $\delta25.757$, $\delta23.337$.

<u>Step 2:</u>

isobutyl benzene

isobutyrophenone

Step 3:

Step 4:

1-chloro-1-(4-isobutylphenyl)ethane

isobutylacetophenone

<u>Step 5:</u>

Fig. 4 Solar heat synthetic pathway to ibuprofen. The synthetic route designed to synthesize ibuprofen via the use of solar energy as the sole heat source



Fig. 5 Solar Friedel–Crafts (isobutylacetophenone) set-up. Solar apparatus set-up to synthesize isobutylacetophenone



Fig. 6 Solar Grignard reaction set-up. Solar apparatus set-up to perform the Grignard reaction to synthesize ibuprofen

1-(4-isobutylphenyl)ethanol synthesis

The synthetic procedure for this step was a modification of the synthesis previously published by Kjonaas et al. [14]. A solution of p-isobutylacetophenone (1.20 mL), methanol (3.00 mL), and sodium borohydride (0.2509 g) was mixed in a separatory funnel and allowed to sit for 10 min. After the standing time period, a 10 % HCl solution (10.0 mL) was added to remove any unreacted sodium borohydride, and the product was extracted using petroleum ether. 1-(4-isobutylphenyl)ethanol product (1.002 g, 87.2 %) was collected and dried using anhydrous sodium sulfate. ¹H NMR (300 MHz, CDCl₃): δ7.281 (2H, m, J = 4.0 Hz), $\delta 7.174$ (2H, m, J = 4.0 Hz), $\delta 4.855$ (1H, s, J = 0.92 Hz), $\delta 2.714$ (3H, q, J = 2.2 Hz), $\delta 2.554$ (2H, t, J = 2.8 Hz), δ 1.795 (1H, q, J = 2.7 Hz), δ 1.484 (1H, m, J = 2.8 Hz), $\delta 0.976$ (6H, q, J = 6.1 Hz). ¹³C NMR (300 MHz, CDCl₃): 143.325, 140.684, 129.143, 125.357, 70.034, 45.196, 30.343, 25.076, 22.725, 22.465.

1-chloro-1-(4-isobutylphenyl)ethane synthesis

The synthetic procedure for this step was a modification of the synthesis previously published by Kjonaas et al. [14]. A solution of 1-(4-isobutylphenyl)ethanol (1.10 mL) was placed into a separatory funnel and mixed with 12.0 M HCl (10.0 mL) for a period of 5 min. The product of the reaction was extracted using petroleum ether. 1-chloro-1-(4-isobutylphenyl)ethane product (0.860 g, 78.8 %) was collected and dried using anhydrous sodium sulfate. ^1H NMR (300 MHz, CDCl $_3$): 87.111 (2H, m, J = 4.0 Hz), 87.104 (2H, m, J = 4.0 Hz), 85.985 (1H, q, J = 0.94 Hz), 83.341 (3H, q, J = 2.0 Hz), 82.701 (2H, t, J = 3.1 Hz), 81.761 (1H, m, J = 2.1 Hz), 80.996 (6H, q, J = 6.1 Hz). ^{13}C NMR (300 MHz, CDCl $_3$): 8197.002,

 δ 146.36, δ 135.169, δ 129.509, δ 128.224, δ 45.227, δ 30.76, δ 25.757, δ 23.337.

Ibuprofen synthesis via Grignard reaction using solar heat source

The synthetic procedure for this step was a modification of the synthesis previously published by Kjonaas et al. [14]. A solution of 1-chloro-1-(4-isobutylphenyl)ethane (0.25 mL), magnesium (0.507 g), THF (10.00 mL) and 1,2-dibromoethane (4 drops) was placed in a dry 50-mL round bottom flask that had been painted black using VHT® Flame Proof paint. No stir-bar was placed into the round bottom flask because refluxing liquid was sufficient to mix the solutions. The flask was attached to the solar reflector in the position that the feed horn of the satellite dish was located to provide the best location for the directed focal point of sunlight (Fig. 6).



Fig. 7 Foaming as evidence of grignard formation. Solar Grignard reaction in process displaying foaming as evidence of the formation of the Grignard reagent

A modified Baum et al. [15] Allign-type condenser, filled with propylene glycol and capped with pipet bulbs to insure that the propylene glycol stayed in the condenser, was attached to the round bottom flask. To ensure that the reaction stayed moisture free, a drying tube filled with calcium chloride was attached to the top of the condenser. The solar heat source was then moved into a position in which it was reflecting sunlight onto the bottom of the round bottom flask. The solution was allowed to heat at reflux temperature (65 °C) for 30 min once there was evidence that the Grignard formation had begun (large amount of foaming present) (Fig. 7). After 30 min of reflux, the solution was moved out of the focal point and the solution was allowed to cool to ambient temperature. Carbon dioxide was bubbled into the reaction mixture for a period of 15 min. This solution was then decanted into a separatory funnel and washed with diethyl ether. The solution was then washed with 10 % HCl (8.00 mL) and mixed for a period of 5 minutes. The aqueous phase was then extracted using diethyl ether and combined with the organic phase. This new organic phase was then washed with 5 % NaOH solution. The aqueous layer from this wash was acidified using 10 % HCl until the solution was acidic to litmus. The aqueous layer was washed with diethyl ether to extract the product. Ibuprofen product (37 mg, 27.2 %) was collected. ¹H NMR (300 MHz, CDCl₃): δ 12.22 (1H, s, J = 3.1 Hz), δ 7.22 (2H, m, J = 8.1 Hz), δ 7.10 (2H, m, J = 7.9 Hz), δ 3.71 $(1H, q, J = 7.2 Hz), \delta 2.44 (2H, t, J = 7.2 Hz), \delta 1.84 (3H, t)$ q, J = 6.7 Hz), $\delta 1.50$ (1H, m, J = 7.2 Hz), $\delta 0.89$ (6H, q, J = 6.6 Hz). ¹³C NMR (300 MHz, CDCl₃): 180.21, 140.77, 136.95, 129.41, 127.22, 45.03, 44.70, 33.13, 22.37, 17.98.

Ibuprofen synthesis via Grignard reaction using electrical heat source

The synthetic procedure for this step was a duplicate of the synthesis previously published by Kjonaas et al. [14]. A solution of 1-chloro-1-(4-isobutylphenyl)ethane (0.25 mL), magnesium (0.510 g), THF (10.00 mL), and 1,2-dibromoethane (4 drops) was placed in a dry 50-mL round bottom flask. The flask was heat using an electric heating mantle. To ensure that the reaction stayed moisture free, a drying tube filled with calcium chloride was attached to the top of the condenser. The solution was allowed to heat at reflux temperature (65 °C) for 30 min once there was evidence that the Grignard formation had begun (large amount of foaming present). After 30 min of reflux, heat was removed and the solution was allowed to cool to ambient temperature. Carbon dioxide was bubbled into the reaction mixture for a period of 15 min. This solution was then decanted into a separatory funnel and washed with diethyl ether. The solution was then washed with 10 % HCl (8.00 mL) and mixed for a period of 5 minutes. The aqueous phase was then extracted using diethyl ether and combined with the organic phase. This new organic phase was then washed with 5 % NaOH solution. The aqueous layer from this wash was acidified using 10 % HCl until the solution was acidic to litmus. The aqueous layer was washed with diethyl ether to extract the product. Ibuprofen product (48 mg, 35.1 %) was collected.. ^1H NMR (300 MHz, CDCl₃): $\delta12.52$ (1H, s, J = 3.1 Hz), $\delta7.28$ (2H, m, J = 8.0 Hz), $\delta7.17$ (2H, m, J = 8.0 Hz), $\delta3.65$ (1H, q, J = 7.1 Hz), $\delta2.47$ (2H, t, J = 7.0 Hz), $\delta1.89$ (3H, q, J = 6.9 Hz), $\delta1.55$ (1H, m, J = 7.2 Hz), $\delta0.91$ (6H, q, J = 6.6 Hz). ^{13}C NMR (300 MHz, CDCl₃): 180.45, 140.77, 136.50, 129.45, 127.25, 45.01, 44.62, 33.19, 22.17, 17.78.

Conclusion

When comparing the reactants used for the synthesis of ibuprofen in this study to the Boots and BHC methods, several intriguing observations can be made concerning the safety hazards for all reactants involved. The BHC method uses several chemicals that are not environmentally friendly including hydrofluoric acid and Raney Nickel. Hydrofluoric acid is a highly corrosive liquid and a contact poison whose vapors can penetrate tissue [16]. Raney Nickel, though not as severe of a health hazard, is a pyrophoric material that must be handled under inert atmosphere [17]. One of the positive features of the BHC method is that there is practically no waste generation for this process and therefore, it has a very good atom economy. The Boots method of synthesizing ibuprofen also consists of several environmentally hazardous reagents. This synthetic pathway utilizes hydroxylamine, which must be handled with care since it can explode upon heating [18]. Furthermore, this reagent is an irritant that can absorb through the skin causing cellular mutations. Through the use of the synthetic pathway to ibuprofen proposed in this manuscript, we have reduced the use of toxic chemicals (along with the elimination of fossil fuel derived electricity use). Reagents that are commonly listed as irritants are still used in this pathway (aluminum chloride, acetyl chloride) [19, 20, 21]. The reagent that poses the most environmental/health concerns throughout this process is hydrazine. Hydrazine is a highly toxic, corrosive liquid that has several adverse health effects [22]. However, in our process, we were able to successfully exchange hydrazine for hydrazine hydrate. The hydrate form is still considered to be hazardous upon human contact, but health hazards are greatly reduced when compared to hydrazine [23].

In the future, we plan on continuing to look at this process to make it more of a green synthetic process by reducing the volume of waste generated by this process and increasing its atom economy. One area of interest in

continuing this project would be the attempted replacement of aluminum chloride in the Friedel–Crafts acylation with a more environmentally friendly alternative. During the process of this reaction, the aluminum chloride is converted to aluminum hydroxide, which is filtered off as a cake of solid waste. Since waste products are generated, this process needs to be modified in order to increase its atom economy. We are also attempting to modify conditions at every step in the synthesis to optimize overall yield.

Furthermore, we plan to continue attempting to extend the efficiency of the solar reflector as a heat source. One area that is currently being investigated is the scalability of the solar reflector. We are attempting to determine if there is a point at which our method of direct solar heating could not provide enough thermal heat to successfully drive chemical reactions to completion. Other well know chemical reactions are also currently being investigated using the solar reflector, as well as multi-step organic synthesis reactions used to synthesize commercial products that are highly valued by the general public. The results of using our solar reflector in other organic synthesis reactions, and its further development is also being studied.

Authors' contributions

BA carried out the synthesis, purification, characterization of the compounds, and aided in drafting the manuscript. GM carried out the GC/MS characterization of the compounds. DS conceived of the study, and participated in its design, aided in the synthesis of the compounds, and helped to draft the manuscript. All authors read and approved the final manuscript.

Acknowledgements

We wish to thank Tennessee Technological University (Student Research Development Grant) for funding this research.

Competing interests

The authors declare that they have no competing interests.

Received: 4 December 2015 Accepted: 25 May 2016 Published online: 06 June 2016

References

 Davies NM (1998) Clinical pharmacokinetics of ibuprofen. The first 30 years. Clin Pharmacokinet 34(2):101–154

- Halford GM, Lordkipanidze M, Watson SP (2012) 50th Anniversary of the discovery of ibuprofen: an interview with Dr. Stewart Adams. Platelets 23(6):415–422
- Nicholson JS, Adams SS GB Patent 971,700, 1964; U.S. Patent 3228831, 1966; U.S. Patent 3,385,886, 1968
- Trost BM (1991) The atom economy—a search for synthetic efficiency. Science 254:1471–1477
- Cann MC, Connelly ME (2000) Real world cases in green chemistry.
 American chemical society, Washington DC, pp 19–24
- Chu S, Majumdar A (2012) Opportunities and challenges for a sustainable energy future. Nature 488(7411):294–303
- Murray H, Swartling D Solar ovens to power/run simple organic reactions. Abstracts of papers, 245th ACS national meeting and exposition, New Orleans, LA, United States, April 7–11, 2013. CHED-1051 2013
- Monroe Lizzie, Swartling Daniel J Using solar energy in the green synthesis of deep eutectic solvents. Abstracts of papers, 243rd ACS national meeting and exposition, San Diego, CA, United States, March 25–29, 2012. CHED-1124 2012
- Agee B, Mullins G, Swartling D (2013) Friedel-crafts acylation using solar irradiation. ACS Sustain Chem Eng 1:1580–1583
- Agee B, Mullins G, Biernacki J, Swartling D (2014) Wolff-kishner reduction reactions using a solar irradiation heat source and a green solvent system. Green Chem Lett Rev 7(4):383–392
- Agee B, Mullins G (2014) Swartling D Use of solar energy for biodiesel production and use of biodiesel waste as a green reaction solvent. Sustain Chem Process 2:21. doi:10.1186/s40508-014-0021-2
- Amin S, Barnes A, Buckner C, Jones J, Monroe M, Nurmomade L, Pinto T, Starkey S, Agee B, Crouse D, Swartling D (2015) Diels-alder reaction using a solar irradiation heat source designed for undergraduate organic chemistry laboratories. J Chem Educ. doi:10.1021/ed500850c
- P3 international corporation. 71 West 23rd street, suite 1201. New York, NY 10010-4102. Tel: 212-741-7289
- Richard Kjonaas A, Peggy Williams E, David Counce A, Lindsey Crawley R (2011) Synthesis of ibuprofen in the introductory organic laboratory. J Chem Educ 88:825
- Baum E, O'Callaghan I, Cinninger L, Esteb J, Wilson A (2013) Static fluid condensers for the containment of refluxing solvent. ACS Sustain Chem Eng 1:1502–1505
- Material Safety Data Sheet Hydrofluoric Acid. http://wcam.engr.wisc. edu/Public/Safety/MSDS/Hydrofluoric%20acid,%2049%25.pdf
- Material Safety Data Sheet Raney Nickel. https://fishersci.com/shop/msdsproxy?storeld=10652&productName=AC395925000
- Material Safety Data Sheet Acetic anhydride. http://www.sciencelab. com/msds.php?msdsld=9927061
- Material Safety Data Sheet Aluminum chloride. http://www.clayton. edu/portals/690/chemistry/inventory/MSDS%20aluminum%20chloride%20anhydrous.pdf
- Material Safety Data Sheet Sodium ethoxide. https://www.fishersci.ca/ viewmsds.do?catNo=AC168590025
- Material Safety Data Sheet Acetyl chloride. http://www.sciencelab.com/ msds.php?msdsld=9927420
- Material Safety Data Sheet Hydrazine. http://www.sciencelab.com/ msds.php?msdsld=9924279
- 23, Material Safety Data Sheet Hydrazine hydrate, http://www.sciencelab.com/msds.php?msdsId=9924280

Submit your manuscript to a SpringerOpen journal and benefit from:

- ► Convenient online submission
- ► Rigorous peer review
- ► Immediate publication on acceptance
- ► Open access: articles freely available online
- ► High visibility within the field
- ► Retaining the copyright to your article

Submit your next manuscript at ▶ springeropen.com