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Study of green approach in organic synthesis

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Abstract

In order to construct dependable, sustainable, and environmentally friendly synthesis processes without producing undesirable or hazardous by-products, green synthesis is necessary. In order to do this, it is crucial to use the most effective solvent systems and natural resources. A number of biological molecules have found a home in metallic nanoparticles synthesized in an environmentally friendly manner.

Keywords: Hazardous, products, green, environmental, synthesis

Introduction

The field of green chemistry has been around for a while. The chemical industry, environmental protection, and chemistry have all seen significant advancements because to this new philosophical approach and the concepts it has introduced and expanded upon. "Utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture, and applications of chemical products" is to put it simply. In 1991, Paul Anastas initially used the term "Green Chemistry" as part of a US Environmental Protection Agency (EPA) special programme that relied on the multidisciplinary collaboration of academic institutions, nonprofit organisations, and government agencies to spur major advances in chemical technology and chemistry. Additionally, the program's stated goal of safeguarding the environment via the reduction or removal of hazards to human health was to influence chemists' worldviews. Launched simultaneously with the first "Green Chemistry" project was the "Alternative Synthetic Pathways" study initiative. A green metric that can quantitatively compare the "greenness" of different products and processes was developed in response to theoretical ideas like Trost's "atom economy" and Sheldon's "E factor," which encouraged new ways of thinking about chemistry.

The use of an established set of guidelines for the

development, production, and use of chemical goods that reduces or eliminates the production of harmful chemicals as green chemistry, sometimes known as sustainable chemistry, and was first presented in 1991 by the eminent scientist Paul Anastas. To my knowledge, no other scientific discipline has ever zeroed focused on the inherent dangers of chemicals or chemical processes. A new paradigm in research, "Green Chemistry" has attracted a lot of global chemists are devoting their creative energies to the development of new synthesis techniques, reaction conditions, analytical instruments, catalysts, and procedures, and are paying close attention to. To honor outstanding achievements in applied green chemistry or technology, the Presidential Green Chemistry Challenge Awards were founded in 1995 and started to be presented in 1996 by the Clinton administration.

New chemical advancements offer new environmental issues and unpleasant unforeseen side effects, despite the undeniable prevalence of chemistry in our everyday lives. As a result, the pharmaceutical and chemical sectors are under persistent pressure to enhance the efficiency and selectivity of synthetic processes while simultaneously decreasing chemical waste. Consequently, sustainability indicators and green chemistry concepts need to be part of educational initiatives in order to achieve more sustainable thinking and the incorporation of sustainability standards

into R&D, manufacturing, and other related fields.

The term "biosurfactants" refers to a class of chemicals derived from plants, animals, and microbes that are amphiphatic and surface active. Biosurfactants are physically and chemically identical to synthetic surfactants in that they both lower surface tension and interfacial tension. Plus, they're superior than synthetic surfactants in many ways.

Materials and Methods

Ramesh *et al.* (2018) ^[1] erbium (III) triflate was synthesized at room temperature using a multi-component synthesis method using 3,4-dihydro-2H-pyran, which served as an effective heterogeneous catalyst in the Hetero-Diels-Alder process. Condensation of substituted styrenes, different β -keto esters, and formaldehyde in a single pot with ethanol as the solvent allows the process to continue. Incredibly, they were able to reuse the catalyst up to 10 times with no change to the activity or reaction time, and the product yields were fantastic.

T. Khan *et al.* (2019) ^[2] presented a simple, effective, and ecologically friendly method for synthesizing aminoimidazo-benzothiazole analogues using a green solvent in a one-pot multi-component reaction involving indole-3-carbaldehyde, 2-aminobenzothiazole, and isocyanide. There are a number of advantages to this approach, including its straightforward technique and workup process, high yields, little environmental impact, cheap acid catalyst, and elimination of column chromatography as a purification step.

Shanmugam Prakash (2018) ^[3] showcased a stable and reusable heterogeneous catalyst (copper oxide nanoparticle). Using ethanol as a solvent, the 3,4-dihydropyrimidinones were prepared quickly and with a high yield using the synthesized nano catalyst. Attractive features include a highly reusable catalyst, increased yields with little effort, and cheap, simple workup.

Mahdiye Foroughi Kaldareh *et al.* (2020) ^[4], created a new magnetic catalyst with nicotinic acid loaded onto cobalt ferrite [CoFe₂O₄@SiO₂@Si(CH₂)₃Cl@NA] that showed promise for the synthesis of substituted chromeno quinoline compounds in a single pot. Starting with a pH higher than 7, the solid cobalt ferrite (CoFe₂O₄) material was made by combining iron and cobalt salts in a 1:1 ratio. After that, tetramethyl orthosilicate was ultra-sonified onto the constructed nanocomposites. The resultant catalyst, CoFe₂O₄@SiO₂@Si-(CH₂)₃Cl, was prepared by preserving the obtained CoFe₂O₄ coated silica nanoparticles with 3-chloropropyltrimethoxysilane. To achieve the catalyst we wanted, we stuck the produced nanoparticles to 4-aminoquinoline. Spectroscopic examinations of the produced material showed noticeable spherical nanoparticles with a diameter of 23 nm, as characterised using scanning electron microscopy (SEM). Crystallite size of 18 nm was verified by P-XRD examination, and the HR-TEM of the catalyst shows very uniformly crystalline spherical nanoparticles with grains of around 20-30 nm. Based on the VSM study, the material's magnetization should be around 27 emu. g⁻¹. Additionally, scaffolds of chromeno-[3,4-b]-quinoline were generated to assess the catalytic effectiveness. 4-Aminocoumarin, active methylene compound, and aldehydes were all included in

the preparation technique in equal proportions. Conventional wisdom was that the combination would undergo cyclization via an intermediate that underwent Knoevenagel condensation. Under reflux conditions, the solid material reduced the reaction time to 1 hour and increased the product yield by almost 95%.

A zinc cation doped λ -carrageenan/Fe₃O₄ composite nano catalyst was prepared by Fariba Keshavarz pour and Hossein Tavakol (2017) ^[5]. This catalyst has the potential to be used in the synthesis of quinoline analogues. A two-stage procedure was used to customize the catalytic composites. At first, λ -carrageenan/Fe₃O₄ nanoparticles were made by mixing λ -carrageenan and magnetite in a 1:1 ratio, and then adding water to make the nanoparticles precipitate. Mesoporous zinc cation doped λ -carrageenan/Fe₃O₄ composite nano catalyst particles are accumulated by sprinkling a zinc chloride solution over the nanoparticles. The catalyst material's superparamagnetic nature was shown at around 70 emu/g by morphological analysis utilising several methods, including a VSM investigation. The catalyst particles were found to have an average size of 16 nm according to TEM examination. FESEM-EDX verified by ICP analysis that the material contains C, O, S, Fe, and Zn elements. The TGA study indicated stability up to 80 °C, while P-XRD showed a very amorphous structure. Novel quinolines were synthesized at 80 °C utilising the synthesized catalyst in a one-pot condensation technique with substituted aldehydes, butanal, and aniline. While FT-IR, H1, and C13 NMR spectroscopy were used to characterise the target molecules, TLC was used to detect when the reaction was complete. Remarkably, product yields ranging from 52% to 95% were achieved in only 15 minutes, demonstrating that the catalyst material significantly enhanced the process. Separation using an external magnetic field also allowed for five successful cycles of catalyst reuse.

Biosurfactant as a sustainable method for the production of biologically important heterocycles

One of the most important things researchers are doing to find ecologically friendly and cost-effective ways to synthesize in this field is to avoid using toxic chemical solvents. Water is one of the most appealing alternatives to organic solvents since it is cheap, easily accessible, non-combustible, non-toxic, and harmless to the environment. However, owing to the low solubility of several organic molecules, chemical reactions in water often have restricted scope. We chose a natural surfactant as the amphiphile for this transformation because it allowed us to create a new catalytic system that could employ water as the reaction medium.

Not only may green chemistry methods help cut down on waste, energy expenses, and by-products, but they can also open up new avenues for working with materials that were previously unavailable. It is possible to define "the Perfectly Green" reaction as one that does not generate any byproducts, is very selective, runs at room temperature, and does not need the use of an organic solvent. Biosurfactants, when used in conjunction with the chemical process, can solve all of these problems. They are a great substitute for volatile organic solvents in greener technologies because they are less toxic, biodegradable, catalyst-friendly, non-

flammable, and non-corrosive. Additionally, their manufacturing might be more cost-effective because of their abundant natural resources.

One kind of heterogeneous system is the interface, and biosurfactants, sometimes called surface active agents, are microbial amphiphilic and polyphilic polymers that have a tendency to interact with this boundary. Biosurfactants are a relatively new technology that has enormous promise for a variety of industrial uses, such as improved oil recovery, lubricants, health care, the food processing sector, and crude oil drilling. There has been a tremendous uptick in the number of comprehensive analyses of the possible uses of these biosurfactants in food, cosmetics, soap, and dermal or transdermal medication delivery systems. Using biosurfactant as a catalyst and reaction medium to speed up organic transformations has received surprisingly little attention, despite their wide range of uses in environmental and industrial biotechnology.

Green chemistry, which uses plant materials in organic

synthesis, is better than chemical approaches since it is cheaper and better for the environment. The fruit of *Balanites roxburghii*, commonly known as Hingota, was selected as the biosurfactant source in this study due to its great natural abundance and low cost. Its price of Rs. 50/- per kg is much lower than that of chemical surfactants. The traditional uses of this plant and its fruit include treating whooping cough, skin illnesses, snake bites, and as an emetic, anthelmintic, anti-fungal, and purgative. This plant was found to include alkaloids, flavonoids, tannins, phenolic compounds, and saponins, according to phytochemical research. Because it contains a number of saponins, the water-based fruit extract of *Balanites roxburghii* has an acidic pH (around 4.86) and shows off a lot of surface activity (Fig. 1). Because of this, we decided to look into the acid-mediated reaction catalytic activity of the water extract. Following a similar line of thinking, we recorded the synthesis of aldimine using an aqueous extract of the pericarp of fruits of *Sapindus trifoliatius* not long ago.

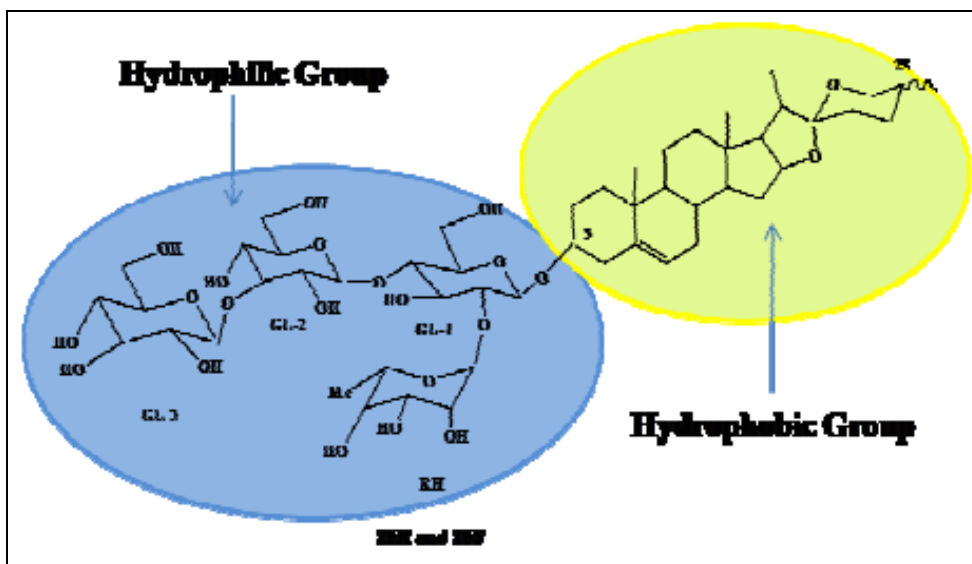


Fig 1: The Saponin Structure

Results and Discussion

A biosurfactant solution derived from *Balanites Roxburghe* fruit was the initial target of this investigation. Dried fruit (20 g) was steeped in 100 mL of distilled water for 12 hours for this purpose. The soaked and filtered material was then

macerated with the water. The filtrate has a stability of at least 30 days when stored below 5 °C. Figure 2 shows the results of diluting this wine-red solution with distilled water to create solutions of several concentrations (% v/v).

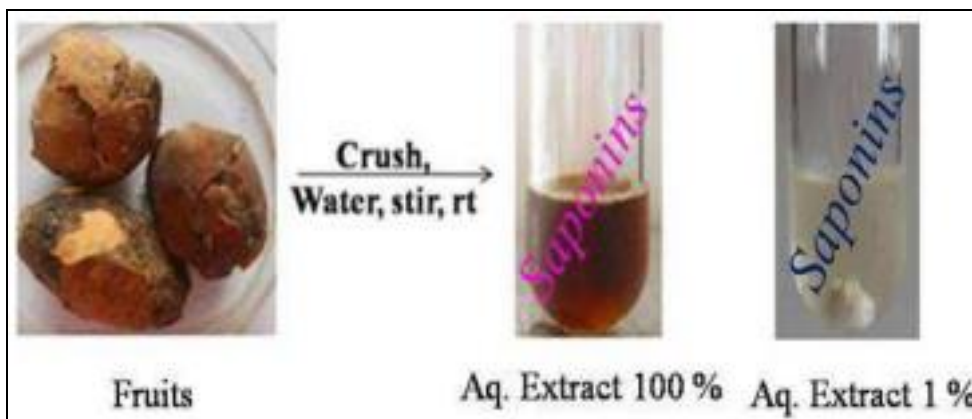
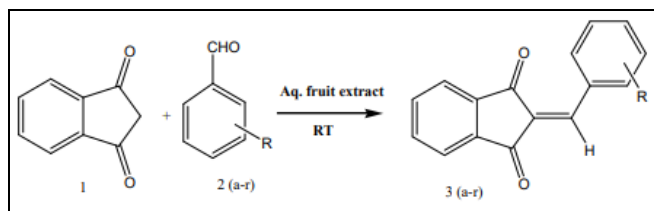


Fig 2: Using *Balanites roxburghii* Fruit to Make a Biosurfactant Solution

To optimise the reaction conditions in the 5 mL of water-based *Balanites roxburghii* fruit extract, 1,3-indanedione 1 (1 mmol) and 2-nitrobenzaldehyde 2h (1 mmol) were added at room temperature (Scheme 3.1.13). The production of coloured precipitates, as seen visually (Fig. 3) and verified by TLC, showed that the reaction had completed. The reaction mixture was diluted with cold water and the product was separated once the reaction was completed, as shown by TLC. The correspondingly pure product, which showed accurate ¹H NMR and ¹³C NMR spectra, was obtained by filtering the reaction mixture and washing with water and ethanol.



Scheme 3.1.13

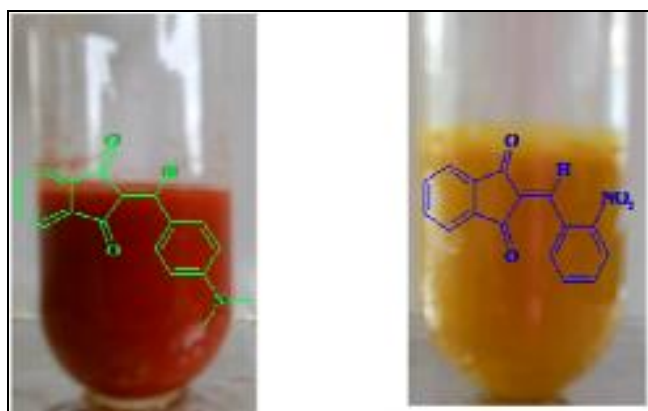


Fig 3: Items that are coloured

Using these findings, we calculated the optimal concentration of the reactants in water for highest product yield during reaction. The aqueous extract of *Balanites roxburghii* fruit was used in the model reaction at room temperature at varying concentrations (% v/v). By diluting the solution with water, several concentrations (% v/v) of solutions were created, with the prepared solution being treated as 100%. Even when the solution was diluted to 1%, there was no discernible influence on the conversion rate of 2-arylideneindane-1,3-diones when the concentration was changed. In order to comprehend this impact, the pH of each solution was evaluated. It was found that, shockingly, the pH of all the solutions stayed the same, suggesting that the fruit aqueous extract functioned as a buffer. The structure of saponins, which are typically amphiphilic molecules with sugars connected to a sterol or a triterpene non-polar group, accounts for the buffering effect of the catalytic solution. Here, the sugar component functions as a buffer, therefore reducing the catalyst concentration by 1% without affecting product yield is possible by diluting the biosurfactant solution with water; this is advantageous since it alters neither the concentration nor the catalytic characteristics of the solution. Sodium dodecyl sulphate (SDS) was also used in the model reaction so that the catalytic activity of chemical surfactant and natural surfactant could be

compared. In terms of both response time and yield, they were identical. Chemical surfactants cannot be recycled, in contrast to natural surfactants which may be used as a buffer system. In addition, the product yield was significantly impacted by the dilution-induced reduction in SDS concentration.

Prolonged reaction durations suggest the biocatalyst plays a crucial role, although a controlled reaction performed in water without a biocatalyst yielded no equivalent product under the same circumstances.

Following concentration optimisation, 1,3-indanedione was added to a 1% aqueous extract of a variety of structurally different aryl aldehydes and let to sit at room temperature (Table 1). Within 5–20 minutes at room temperature, the reactions were completed, producing the target compounds in high concentrations. There were no problems with the reactions carried out on the aryl aldehydes that had electron-donating and electron-withdrawing groups. Also, heteroaromatic aldehydes like furfuraldehyde and thiophene-2-aldehyde interacted well, producing the desired compounds in good quantities. Also, 1-naphthaldehyde, which is sterically inhibited, may be handled using this approach. No abnormalities were detected in any of the instances where 2-arylideneindane-1,3-diones were the only products. After recrystallization in ethanol, the pure products were characterised using physical constants and spectral methods.

Table 1: Aqueous extract of *Balanites roxburghii* fruit catalyses the production of 2-arylideneindane-1,3-diones.

Sr. No.	Aldehyde (2a-2r)	Product (3a-3r)	Time (min)	Yield ^b (%)	M. P. [Lit.] ^c (°C)
1	Ph	3a	5	93	150 [152-153] ³⁵
2	4-Me-C ₆ H ₄	3b	15	92	150 [150-151] ³³
3	4-OMe-C ₆ H ₄	3c	20	89	155 [156-157] ³³
4	4-Cl-C ₆ H ₄	3d	5	92	180 [180-182] ³⁶
5	4-F-C ₆ H ₄	3e	5	90	170 [170] ³⁴
6	2-OH-C ₆ H ₄	3f	12	88	194 [193-195] ³⁶
7	4-OH-C ₆ H ₄	3g	10	90	241 [241-243] ³⁶
8	2-NO ₂ -C ₆ H ₄	3h	5	94	190 [192-194] ³⁶
9	4-NO ₂ -C ₆ H ₄	3i	17	94	232 [234-236] ³⁶
10	1-naphthyl	3j	10	83	172 [174-176] ³⁵
11	4-N(Me) ₂ -C ₆ H ₄	3k	20	88	178 [180] ³⁴
12	4-OH, 3-OMe-C ₆ H ₃	3l	15	93	218-220
13	3, 4, 5-(OMe) ₃ -C ₆ H ₂	3m	18	92	185 [185] ³⁴
14	Furyl-2-yl	3n	5	90	210 [209-211] ³⁵
15	Thiophene-2-yl	3o	5	94	178-180
16	2-CHO-C ₆ H ₄	3p	5	92	218-220
17	4-Br-C ₆ H ₄	3q	5	90	173-175
18	4-CN-C ₆ H ₄	3r	5	93	238-240

^a Atomic analysis, infrared spectroscopy, and nuclear magnetic resonance (NMR) spectroscopy were used to characterize all of the products.

^b Isolated yields.

^c Literature values in parenthesis.

The capacity of biosurfactant, an aqueous extract of *Balanites roxburghii* fruit, to create micelles in water may explain its very high catalytic activity. The hydrophobic environment helps the reactant molecules to agglomerate, which speeds up the process. This causes a rise in the rate of reaction by increasing the effective concentration of organic substrates. Micellar solutions are able to efficiently and effectively collide because to their hydrophobic interior,

which draws out any water that may have been produced as a byproduct of the reaction. This allows the equilibrium to be shifted towards the creation of products with high yield.

Its remarkable solubility in the reaction mixture was another remarkable property of biosurfactant. Nearly all of the biosurfactant was extracted from the water solution after the reaction was finished since it is more soluble in water than in organic solvents. After adding water to the reaction mixture, the product that precipitated out was easily separated by filtering. Over the course of four reaction cycles, recycling tests were conducted using 2-nitrobenzaldehyde and 1,3-indanedione as substrates to evaluate the biosurfactant's reusability. Following each experiment, the catalyst aqueous solution was filtered out, rinsed with diethyl ether, concentrated, and re-run with new reactants following the same reaction conditions. The extraordinary reusability and recycling of the catalytic solution was seen without any change in product yield, which is an indication of its 'in-flask' recyclability. This finding is rather intriguing. The catalytic solution acts as a buffer, which is responsible for this.

Product characterization

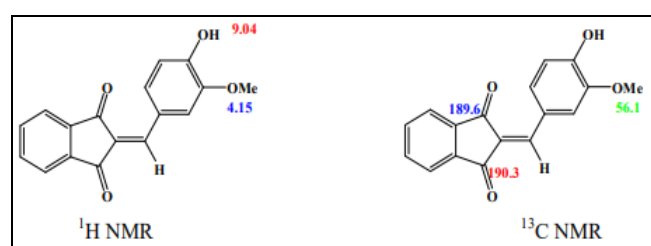


Fig 4: Indene-1,3-dione, which is 2-(4-hydroxy, 3-methoxybenzylidene)

The hydroxyl group's distinctive peak in the infrared spectrum (Fig. 4) was seen at 3453 cm⁻¹. At 1715 and 1672 cm⁻¹, two carbonyls were detected. Three protons of the methoxy group showed a strong singlet at δ 4.15 ppm in the ¹H NMR spectrum (Fig. 5). From δ 6.27-8.01 ppm, the olefinic proton and the other aromatic protons echoed. At δ 9.04 ppm, there is a hydroxy proton doublet. The signal in the aliphatic region of the ¹³C spectrum (Fig. 6) was caused by the presence of methoxy carbon at 56.1 ppm. At δ 114.5, 115.1, 122.9, 123.1, 126.1, 126.6, 132.2, 134.6, 134.8, 140.0, 142.4, 146.3, 147.7, 151.2 ppm, the remaining carbons were observed in the aromatic zone. Two carbonyl carbon signals, at 189.6 and 190.3 ppm, respectively, correlate to.

(Table 1, Entry 16) 2-((1,3-dioxo-1H-inden-2(3H)-ylidene) methyl) benzaldehyde

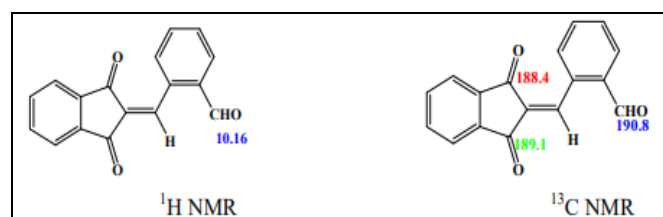


Fig 5: Showed a strong singlet at δ 4.15 ppm in the ¹H NMR spectrum

a ring containing two carbon atoms fused together(2H-indene-1,3-dione) (Entry 18 in Table 1)

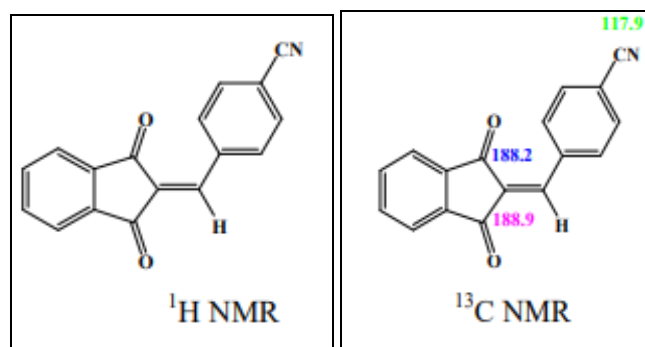


Fig 6: The signal in the aliphatic region of the ¹³C spectrum

Conclusion

With the emphasis on the adoption of cleaner green chemistry processes and concerns over the environmental impact of using volatile organic solvents (VOCs), the potential of water or non-classical solvents has become highly relevant. In addition to its abundance and for economical and safety reasons, water has naturally become a substitute and an environmentally benign solvent in organic synthesis.

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