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DEVELOPMENT OF GREEN CHEMISTRY METHODS FOR ORGANIC SYNTHESIS

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Abstract

When it comes to the search for environmentally responsible methods in the workplace and in laboratories, the discipline of green chemistry has become an increasingly significant field. With the goal of minimizing the negative effects on the environment while simultaneously improving safety and efficiency, this field of study focuses on the development of chemical products and processes that decrease or eliminate the use of hazardous compounds and the manufacture of such substances. Organic synthesis, which is an essential component of both chemical research and industry, has traditionally involved the use of techniques that have the potential to be hazardous to both human health and the environment. Significant progress has been achieved in the direction of making organic synthesis more environmentally friendly by the incorporation of the concepts of green chemistry. These principles include the prevention of waste, the utilization of safer solvents and renewable feedstocks, energy efficiency, and eco-friendly atom economics. The purpose of this study is to investigate current advancements in green chemistry methodology, including the utilization of non-toxic catalysts, alternative solvents, energy-efficient techniques, and renewable feedstocks. Additionally, the research will analyze the obstacles that this developing subject has as well as the potential future paths that it may go. The transition that is currently taking place, which is being driven by green chemistry, has the possibility of making the chemical sector more responsible and sustainable.

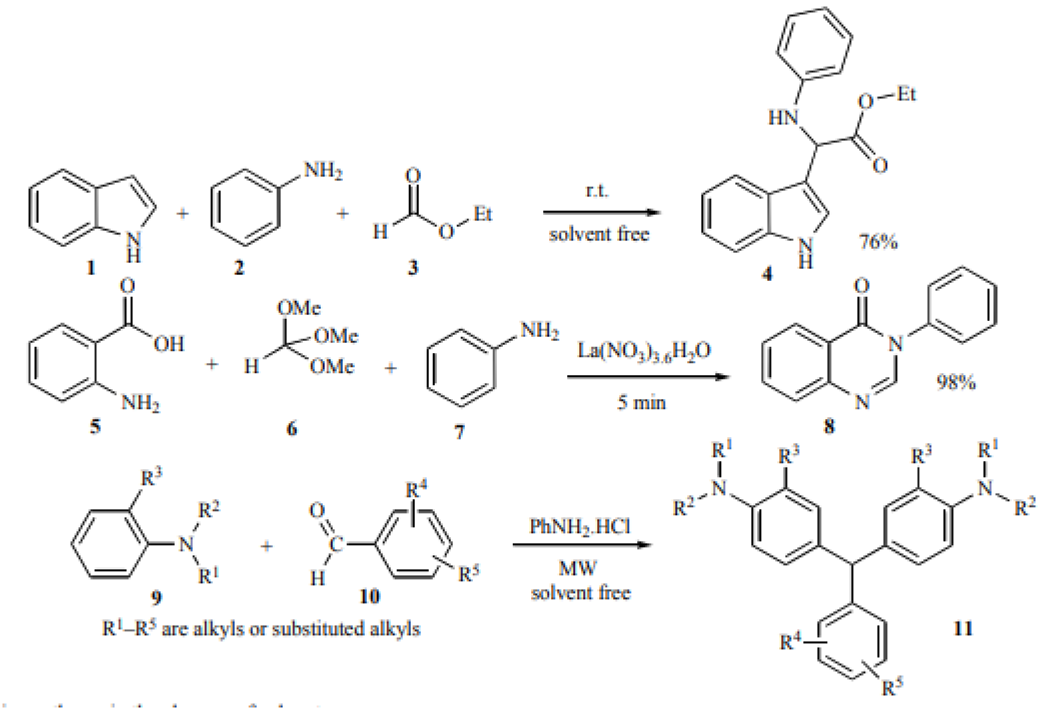
Keywords: *Green Chemistry, Organic, Synthesis*

Introduction

With the urgent need to reduce the negative impact that chemical processes have on the environment and to improve their sustainability, the rapidly developing subject of green chemistry has arisen as a crucial component of modern chemical research and industry. The objective of green chemistry, which is often referred to as sustainable chemistry, is to develop chemical processes and products that reduce the amount of harmful compounds that are used and produced. This field of study also strives to increase safety and efficiency across a variety of industries, in addition to concentrating on lowering the ecological footprint that chemical operations leave behind. However, the origins of the notion of green chemistry may be traced back to the growing consciousness of the environment that occurred in the 1960s and 1970s. The formal expression of the concept occurred in the early 1990s. An important turning point occurred in 1962 when Rachel Carson's book "Silent Spring" was published. This book brought attention to the harmful effects that pesticides have on both the environment and the health of other people. The United States Environmental Protection Agency (EPA), which was established in 1970, was one of the environmental rules and agencies that came into existence during this time period. It was instrumental in the formation of the principles that govern environmentally responsible chemical techniques.

WHAT IS GREEN CHEMISTRY?

Anastas [1, 2] was the first person to use the phrase "Green Chemistry" in 1991. This was done as part of a special program that was developed by the United States Environmental Protection Agency (EPA) with the intention of encouraging a significant advancement in the field of chemistry and chemical technology. As far as human health is concerned, the program was also intended to change the perspective of chemists and to safeguard the environment by concentrating on reducing dangers or eliminating them entirely. In addition, the program was designed to protect the environment completely. In order to provide a thorough illustration of green chemistry, Anastas and Warner [1-3] suggested a set of twelve principles that can be used with this approach. These principles offer guidelines for expert chemists regarding the synthesis of new compounds, new syntheses, and new technological procedures. These instructions are intended to be followed closely. One of the fundamental concepts of Green Chemistry is the preservation of the environment against pollution, which is described in the first principle. The remaining principles concentrate on issues such as the atom economy, toxicity, solvents, energy consumption, the utilization of raw materials derived from renewable resources, and the usage of renewable resources.



Scheme 1. Synthesis of organic compounds without the use of a solvent.

THE CONCEPT OF GREEN CHEMISTRY

A general scientific program that originated from the inter-disciplinary collaboration of research groups in universities, independent research groups, scientific societies, and government agencies, with members of each of these bodies having their own program dedicated to lowering levels of environmental pollution, the Green Chemistry concept emerged in the United States of America as a general scientific program. "Green Chemistry" refers to a novel approach to the synthesis, processing, and use of chemical substances, with the goal of reducing the risks to human health and the pollution of the environment. The chemical products are broken down into simple, non-toxic compounds that are compatible with the environment through the process of decomposition.

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THE 12 PRINCIPLES OF GREEN CHEMISTRY

1. Prevention

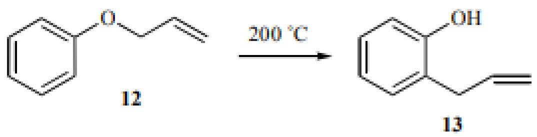
It is better to prevent the formation of waste materials and/or by-products than to process or clean them.

Synthesis of organic compounds while solvents are not present. The use of this principle has led to the development of a field of chemistry known as "grinding chemistry," in which the reagents are combined without the use of a solvent, maybe by simply grinding them in a mortar. When applied to indoles, Chen et al. provided a nice illustration of a Friedel–Crafts reaction that involves three components and results in the formation of functionalized indole 4. Using a method that did not require the use of a solvent, Venkateswarlu and colleagues developed a synthesis of 4-quinazolinone 8 comparable to the one described above. A recent review was conducted on the topic of "grinding chemistry." The application of microwaves to irradiate mixtures of plain reagents is becoming an increasingly popular area of chemistry that does not entail the use of solvents. The production of 4,4'-diaminotriphenylmethanes (11) through the use of microwave irradiation is an illustration of this method (Scheme 1).

Atom Economy

Synthetic methods should be designed in such a way that all products participating in the reaction process are included in the final product.

Chemical experts from all around the world agree that a reaction is considered to be "perfect" when the yield is at least 90 percent. On the other hand, this kind of reaction might result in a significant amount of excess waste. Trost is the one who came up with the idea of an atom economy, which might be depicted as follows: % atom economy equals (FW of the atoms used) divided by (FW of the reactants in the reaction) multiplied by 100 hundred.



Scheme 2. Allylic rearrangement with 100% atom economy.

Due to the fact that all of the reactants are incorporated into the final product, this reaction has an atom economy of one hundred percent (Scheme 2).

$$\underset{14}{CH_3CH_2COOC_2H_5} + \underset{15}{CH_3NH_2} \longrightarrow \underset{16}{CH_3CH_2CONHCH_3} + \underset{17}{CH_3CH_2OH}$$

Scheme 3. Preparation of an amide with 65.4% atom economy.

In the reaction described above (Scheme 3), the leaving group (OC2H5) and a proton from the methylamine (15) are not utilized in any given reaction. All of the remaining atoms are put to use, and for the following reason:

% atom economy = 87.106/133.189 100 = 65.40%

Designing Safer Products

Product design should prioritize both human and environmental safety.

In 1961, West Germany became the first country in the world to launch thalidomide (20), which is an example of a medicine that is considered to be harmful. For the purpose of preventing nausea and vomiting in pregnant women, this medication was administered. Women who were pregnant and had taken the drug gave birth to children who were born with a disorder known as phocomelia. This condition is characterized by abnormally small limbs, with toes emerging from the hips and arms that resemble flippers. Other infants were born with abnormalities in their eyes and ears, as well as internal organs that were deformed, such as non-segmented small or large intestines. This medication is now being used for the treatment of patients who have multiple myeloma as well as for the acute therapy of the cutaneous signs of erythema nodosum leprosum.

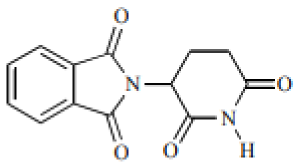


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Fig. (1). Chemical structure of Thalidomide – 2-(2, 6-dioxopiperidin-3-yl)- 1,3-dione.

The insecticide known as spinosad (21), which is very selective and favorable to the environment, was developed by Dow AgroSciences. It is not common for a biological product to exhibit both quick contact and ingestion activity in insects, yet spinosad does both of these things quite frequently (Fig. 2). Spinosad has a positive profile with regard to the environment. In addition to not leaching, bioaccumulating, volatilizing, or remaining in the environment, it does not persist. The photochemical degradation of spinosad will occur when it is exposed to light after it has been applied. Due to the fact that spinosad has a high capacity for adsorption, it does not leach through the soil and into the groundwater when it is used appropriately, therefore buffer zones are not normally necessary. Although spinosad is moderately toxic to fish, it poses a lower risk to fish when compared to several synthetic insecticides that are now in use. Spinosad has a relatively low toxicity to mammals and birds, and although it is moderately toxic to fish, this toxicity implies a reduced risk to fish. 70–90% of the total population

Table 1. Atoms Utilized and Excessive from the Reactants in the Amide Preparation Displayed in Scheme 3

Reactants		Used		Unused	
Formula	FW	Formula	FW	Formula	FW
$C_5H_{10}O_2$	102.132	C_3H_5O	57.057	C_2H_5O	45.061
CH_5N	31.057	CH_4N	30.049	H	1.008
Total $C_6H_{15}NO_2$	133.189	C_4H_9NO	87.106	C_2H_5OH	46.069

Green chemistry is based on the notion that the most essential principle is to eliminate or at the very least reduce the development of hazardous products, which can be harmful to the environment or dangerous to the organisms that live in it.

Principles of Green Chemistry

In 1998, Paul Anastas and John Warner formulated the fundamental ideas that underpin green chemistry and contributed to their codification. Scientists in the field of chemistry can use these Twelve Principles as a guide to build chemical products and processes that are more environmentally friendly. The elimination of waste, the development of safer chemicals and products, the utilization of renewable feedstocks, and the implementation of energy-efficient processes are some of the fundamental principles that contribute to ecological sustainability. Chemists have the ability to drastically lessen the negative effects that the production of chemicals has on the environment and on people's health if they adhere to these principles.

The Role of Organic Synthesis

An essential component of both the field of chemical research and the business world is organic synthesis, which refers to the process of generating more complex organic compounds from simpler ones. In the fields of materials science, agrochemicals, and pharmaceuticals, it is an essential component in the development of these fields. The conventional approaches to organic synthesis frequently include the use of potentially harmful chemicals, solvents, and conditions, which ultimately results in serious environmental and safety concerns. The incorporation of green chemistry principles into organic synthesis is an attempt to address these concerns by inventing methods that are more effective, safer, and less harmful to the environment.

Green catalysis in organic synthesis

The development and application of novel catalysts and catalytic systems achieves the twin goals of ecological preservation and economic gain, making green catalysis an essential component of green chemistry, particularly in organic synthesis. The use of catalysis in green chemistry has many benefits, such as reduced energy requirements, catalytic activity against stoichiometric quantities of materials, improved selectivity, less processing and separation agents needed, and the ability to utilize less hazardous compounds. There are two main categories of catalysis: homogeneous catalysis, in which the catalyst is a liquid and the reaction mixture is also a liquid, and heterogeneous catalysis, in which the catalyst is a solid or a gas and the reaction mixture is a liquid or a gas. As with enzyme catalysis, one of the key benefits of homogeneous molecular catalysts under optimal conditions is the spatial separation of their active sites. One of the main tenets of Green Chemistry is the elimination of the need for distillation or extraction by means of bi-functional phenomena involving reactant activation over between support and active phases; heterogeneous catalysis specifically addresses this goal. It is possible that clays and zeolites, which are environmentally beneficial, will replace the more dangerous catalysts that are now in use.

Chemical reaction systems that do not include a solvent are known as dry media reactions, solid-state reactions, or solvent less reactions. The reactants could be used singly or combined with additional catalytic substances such as clays, zeolites, silica, alumina, or others to carry out a solvent-free or solid-state reaction. The reaction can be triggered by a thermal process or by irradiation with ultraviolet, microwave, or ultrasonic radiation (sonochemical technique). The obvious environmental and financial benefits of solvent-free reactions stem from their ability to streamline experimental procedures, improve work-up skills, and cut down on reaction times. Particularly in manufacturing, this would be crucial. The byproducts of reactions that take place in solid states are not always the same as those that occur in solution phases. The reason behind this is that the interacting molecules in the crystalline phase are packed in a certain way. This is true for crystals formed by a single chemical as well as for solids formed by cocrystallization of two or more molecules of the reactant. It is extremely difficult to conduct organic reactions without using a catalyst and potentially harmful solvents. A better, more environmentally friendly option for chemists is catalyst-free synthesis of different chemical molecules. Green and alternative techniques in organic synthesis include heat processing and irradiation with ultraviolet (UV), microwave (see unit II), or ultrasound (sonochemical method). Unit II explains how to synthesize organic compounds using microwaves. What follows is a condensed version of the sonochemical method.

Sonochemistry as a Green and Alternative Technique in Organic Synthesis

To perform chemical reactions without the need of solvents, sonochemistry is a valuable technique. Some of the primary benefits of these sonochemical methods include high yields with little energy use, minimal waste, and the elimination of solvents. Figure 1 shows how acoustic cavitation, a physical phenomena, is used to activate chemical processes in solution by the use of ultrasound. Cavitation occurs when the attraction interactions between molecules in a liquid are destroyed by mechanical stimulation. Ultrasound causes the liquid to be compressed before it undergoes rarefaction, or expansion, when a rapid decrease in pressure causes the formation of tiny, pulsating gas bubbles. As the ultrasonic energy cycles through them, these bubbles swell until they become unstable, at which point they may smash or collapse violently.

Old Synthesis of Ibuprofen

In the year 1960, the pharmaceutical company Boot (England) was responsible for the synthesis of ibuprofen, which was then marketed and sold under the brand names Aspro, Panadol, and Nurofen. Ibuprofen was manufactured by a process that consisted of six stages, each of which resulted in the generation of secondary by-products and trash. According to the scientists who were working at the time, the most significant issue was that this synthesis had a very "poor atom economy."

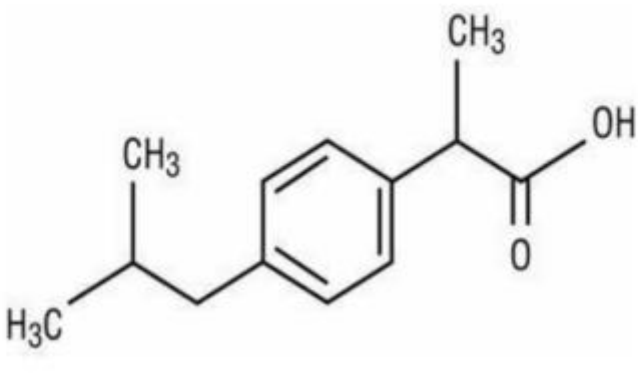

Figure: 2 Ibuprofen

A brand novel synthetic method that consists of only three steps and has high levels of efficiency. In order to reduce the amount of waste produced by the reactions, the atoms of the starting chemicals are integrated into the products of the reactions. When it comes to both synthetic processes, the starting ingredient is 2-methylpropylbenzene, which is a byproduct of the petrochemical sector. Step two of the new method was where the novelty in the method was found. Utilizing a catalyst made of nickel (Raney nickel) resulted in a significant reduction in the number of steps involved in the synthesis process. According to the traditional method of synthetic synthesis, each stage had a yield of 90%, which resulted in the final product having a yield of 40% in comparison to the initial chemical. Because of this, there was an increase in the amount of waste that was produced as by-products. We are aware that a significant number of chemicals were thrown away as waste during the production of the medicine, which was carried out on an annual basis in Great Britain in quantities of three thousand tons. The low efficiency of the reaction mechanism resulted in the loss of energy during the process. In the "greener" technique, which consists of three phases, the final yield is 77%, whilst the Raney nickel catalyst (Nickel, CO/Pt) can be recycled and reused. During the previous method of synthesis, the AlCl3 that was utilized as a catalyst was required to be discarded as waste. It was shown that the second method had significantly reduced energy requirements compared to the first way. Not only from the perspective of economic efficiency, but also from the perspective of more efficient science and technology methods, the new synthetic route of ibuprofen is a classic example of how Green Chemistry principles can influence to the better the industrial synthetic methods. This is true not only from the point of view of more effective science and technology methods.

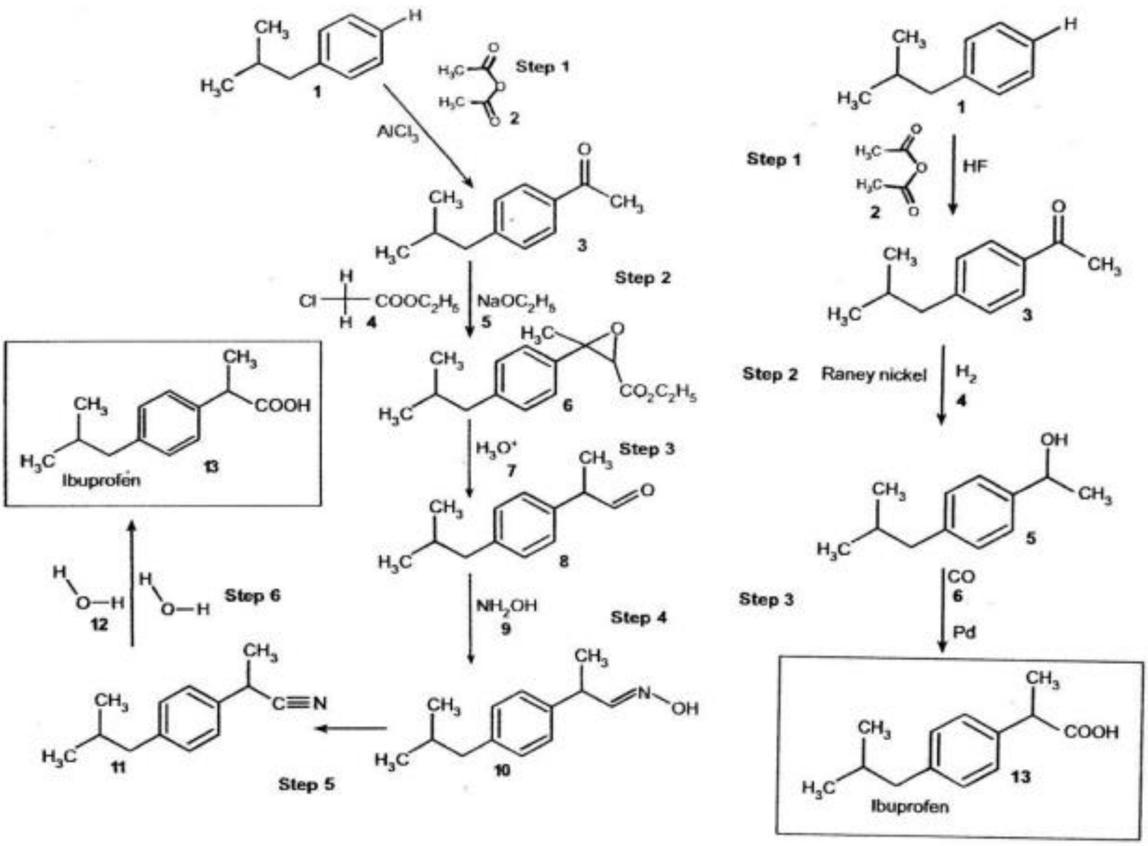

Figure: 3 ibuprofen made by two different synthetic methods

New Synthesis of Adipic Acid

Cakehole and Nylon-6,6 are two materials that are utilized in the pharmaceutical and pesticide sectors. Adipic acid is a highly significant starting material for both of these chemical compounds. Adipic acid is manufactured on an annual basis in quantities exceeding two billion kilograms. The manufacture of adipic acid in industrial settings began with the use of benzene as the starting ingredient. As well as being a solvent, benzene is one of the fundamental compounds that are used in industrial reactions. It is common knowledge that the industry of petrochemicals is primarily responsible for the refining processes that are involved. Moreover, benzene is well-known for its carcinogenic qualities, as it is known to induce leukemia in workers who are highly exposed to it. After that, the initial substance was transformed into cyclohexanone or a combination of cyclohexanone and cyclohexanol. Nitric acid was utilized in the oxidation process, which resulted in the emission of poisonous fumes of nitric oxides, also known as NOx. These fumes in addition to contributing to the warming effect and the destruction of the ozone layer in the stratosphere, were produced. It was unavoidable that the procedure would need to be modified once more, this time using reactions that were less harmful to the environment. Finally, synthetic organic chemists and chemical engineers collaborated to conduct research on potential alternatives. With the "greener" process of producing adipic acid, a new generation of catalysts is utilized. It is cyclohexene that serves as the starting chemical, and hydrogen peroxide (H2O 2) at a concentration of thirty percent is used to oxidize it. In order to dissolve the catalyst, a specialized organic solvent known as Aliquat 336 is utilized. Tungsten catalysts (Na2WO4 / KHSO4 / Aliquat 336), which are a salt of the metal Wolframs or Tungsten (W), are the catalysts in question.

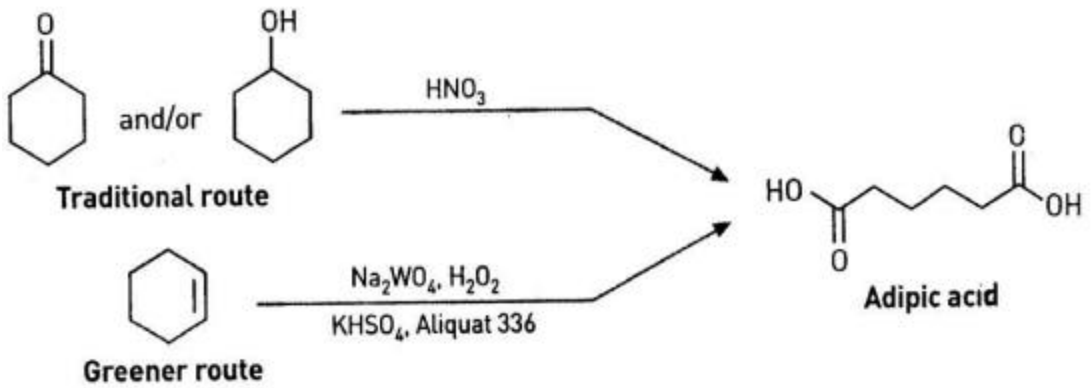

Figure: 4 adipic acid

Conclusion

A huge step forward in the quest for sustainable and eco-friendly chemical procedures has been the incorporation of green chemistry concepts into organic synthesis. Green chemistry presents a revolutionary alternative to conventional chemical synthesis techniques by focusing on waste reduction, safer solvent use, renewable feedstocks, energy efficiency, and an enhanced atom economy. It is now feasible to minimize the environmental and health implications of chemical processes while still achieving great efficiency and selectivity, thanks to recent advancements like the use of non-toxic catalysts, greener solvents, and energy-efficient procedures. In order to make the chemical industry a safer place to work and lessen its impact on the environment, these innovations are essential. The broad implementation of green chemical procedures still faces obstacles, notwithstanding the advancements. These encompass the following: the development of environmentally friendly technologies that are both affordable and easy to scale; the incorporation of green chemistry concepts into school curricula; and the creation of regulatory frameworks that are conducive to these efforts. To overcome these obstacles, we need strong public-private collaborations, multidisciplinary research, and constant innovation. The field of green chemistry has great potential in the field of organic synthesis in the future. The creation of more environmentally friendly synthetic processes stands to benefit greatly from recent developments in biotechnology, computational chemistry, and machine learning. To achieve a more sustainable and responsible future, the chemical industry must embrace green chemistry as it evolves further. To sum up, creating more environmentally friendly ways of organic synthesis through green chemistry is an important scientific effort that will help make our planet a better place for future generations. Environmental preservation, resource efficiency, and society's well-being can all benefit greatly from the chemical community's adoption of these concepts. Although there is still a long way to go, green chemistry holds enormous promise for transforming the chemical industry and solving worldwide environmental problems.

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