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GREEN CHEMISTRY–BASED ENVIRONMENTALLY CLEAN METHODS OF ORGANIC SYNTHESIS

Arzu Mammadova, Aysura Quluzada, Salima Ovchiyeva,
Bibixanım Mammadova, Zeynab Agazada
Sumgait State University, Sumgait, Azerbaijan

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This article provides a comprehensive scientific analysis of the fundamental principles of green chemistry and their application in modern organic synthesis. Green chemistry, introduced by Paul Anastas and John Warner in the 1990s, aims to minimize the environmental impact of chemical processes by reducing waste, lowering energy consumption, avoiding hazardous substances, and promoting economic efficiency. The study examines the twelve principles of green chemistry and demonstrates how these guidelines support sustainable reaction design across all stages of organic synthesis—from raw material selection to final product formation. Various eco-friendly synthesis methods such as microwave-assisted reactions, ultrasonic cavitation, water-based processes, biocatalysis, ionic liquids, supercritical CO_2-mediated synthesis, photocatalysis, and mechanochemistry are analysed in detail. These methods exhibit significant advantages over conventional techniques, including higher yields, reduced toxicity, lower energy requirements, and minimal waste generation. Practical examples, such as the green synthesis of ibuprofen and aspirin, illustrate the industrial and laboratory relevance of these strategies. The findings highlight that green chemistry not only enhances environmental sustainability in the chemical and pharmaceutical industries but also offers promising prospects for future development, especially when integrated with nanotechnology, artificial intelligence, and automated synthesis platforms. Overall, the principles and methods of green chemistry provide an effective scientific framework for addressing global environmental challenges such as climate change, resource depletion, and hazardous chemical waste.

Keywords: green chemistry; organic synthesis; sustainable methods; environmentally friendly processes

INTRODUCTION

Green chemistry is a field developed to minimize the negative environmental impacts of traditional chemical processes [19]. This concept was first introduced by Paul Anastas and John Warner in the 1990s [2]. The main goal of green chemistry is to prevent waste generation, reduce energy consumption, minimize the use of hazardous substances, and ensure that chemical processes are economically efficient [1]. Organic synthesis constitutes a major part of the chemical industry, and traditional methods require large amounts of solvents, catalysts, and high temperatures, all of which can harm the environment. Green chemistry principles offer environmentally friendly alternatives for organic synthesis [8]. This article provides a detailed explanation of the twelve principles of green chemistry and illustrates modern organic

E-mail address: aysuresakir@gmail.com

synthesis methods based on these principles with practical examples. Accordingly, it presents sustainable approaches that can be applied in both industrial and laboratory settings.

Green chemistry principles are applied at all stages of organic synthesis - from the selection of raw materials to the formation of the final product [20]. For example, the use of biodegradable solvents, renewable feedstocks, and low-energy reaction conditions reflects the essence of these principles [14]. In the modern era, issues such as global warming, waste management, and resource scarcity bring green chemistry to the forefront. The application of these principles in organic synthesis not only protects the environment but also increases economic efficiency [6].

EXPERIMENTAL

The 12 principles defined by Paul Anastas and John Warner form the foundation of green chemistry (Figure 1). These principles serve as a guiding framework for designing environmentally friendly methods in organic synthesis [1].

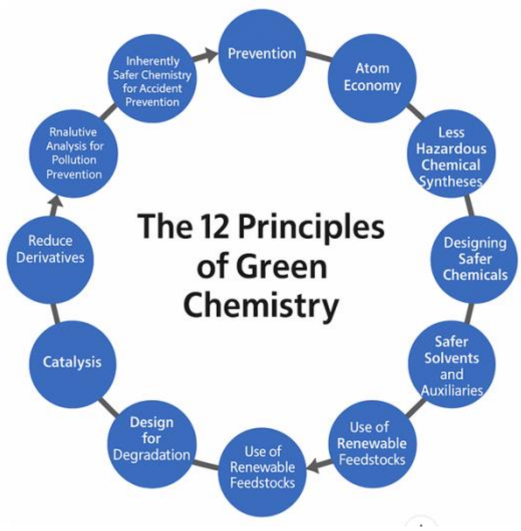

Figure 1. The 12 Principles of Green Chemistry.

The first principle is the prevention of waste. In conventional synthesis, large amounts of waste are generated after reactions, whereas green chemistry recommends eliminating such waste at its source [2]. The second principle is atom economy, which ensures that the atoms used in a reaction are incorporated into the final product to the greatest extent possible [17]. The third principle involves designing less hazardous chemical syntheses, meaning that toxic reagents should be avoided [2]. The fourth principle is the design of safer chemicals; products should be functionally effective while posing minimal harm to human health and the environment. The fifth principle emphasizes safer solvents and auxiliaries, recommending alternatives such as water, ionic liquids, or supercritical carbon dioxide instead of traditional organic solvents like chloroform or benzene [15]. The sixth principle focuses on energy efficiency, encouraging reactions to be carried out at ambient temperature and pressure whenever possible [14]. The seventh principle promotes the use of renewable feedstocks, favoring plant-based materials over petroleum-derived ones [6]. The eighth principle is the reduction of unnecessary derivatization, minimizing the use of protecting groups. The ninth principle highlights the superiority of catalytic reagents, recommending catalysts over stoichiometric reagents to reduce waste [17]. The tenth principle calls for the design of degradable products that break down into harmless substances after use. The eleventh principle involves real-time analysis to prevent pollution, ensuring that reactions are monitored to avoid the formation of hazardous intermediates [12]. The twelfth principle promotes inherently safer chemistry to prevent accidents by minimizing risks such as explosions or toxic exposures [1].

These principles are integrated into organic synthesis to create sustainable processes. For example, the principle of atom economy can increase reaction efficiency by up to 90%.

Organic synthesis methods based on the principles of green chemistry employ various technologies. One such method is microwave-assisted synthesis [4]. Microwave irradiation accelerates reactions and reduces energy consumption. Reactions that would normally require several hours under conventional heating can be completed within minutes using microwave irradiation [7]. For example, in the Diels–Alder reaction, the microwave-assisted method can achieve up to 95% yield while minimizing solvent use [11].

Another method is ultrasonic synthesis. Ultrasonic waves generate a cavitation effect, which increases the reaction rate (Figure 2). In esterification reactions, the use of ultrasound eliminates the need for acid catalysts, thereby reducing waste [8]. Water-based synthesis aligns with the fifth principle of green chemistry, as water is inexpensive, safe, and readily accessible. Phase-transfer catalysts are employed for hydrophobic reagents [3]. For example, in aldol condensation, the reaction can be carried out in an aqueous medium, and the product can be easily separated [15].

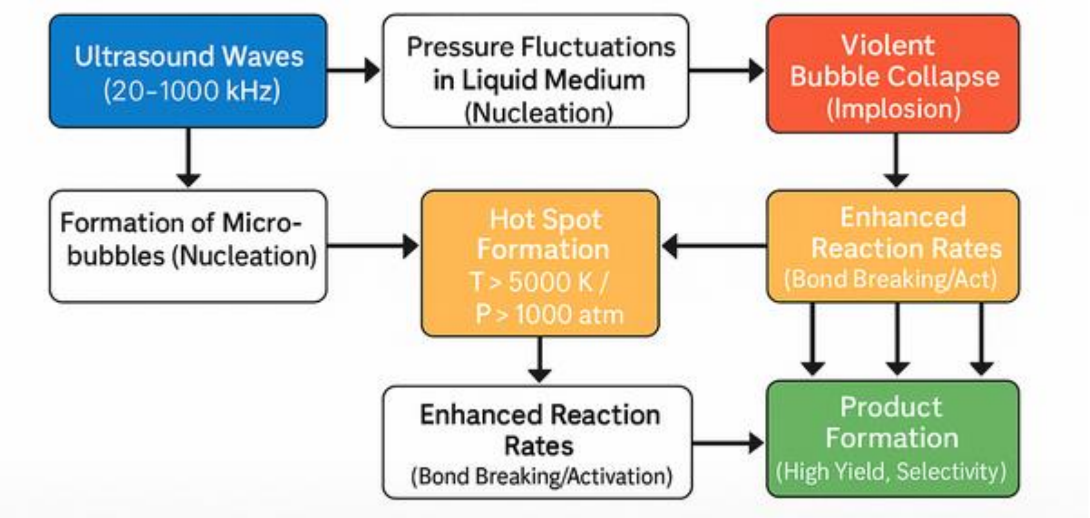

Figure 2. Mechanism of Ultrasonic Cavitation.

Biocatalysis involves the use of enzymes. Enzymes exhibit high selectivity and operate efficiently at room temperature [5]. Ester synthesis using lipase enzymes produces a cleaner product compared to traditional acid-catalyzed methods [16]. The use of renewable feedstocks—such as bioethanol or plant oils—reduces dependence on petroleum-based resources. Biodiesel production is one such example: through transesterification, plant oils are converted into diesel fuel [18].

Ionic liquids are used as solvents. These liquids possess very low vapor pressure and can be recycled. In Friedel–Crafts alkylation, ionic liquids replace the traditional $AlCl_3$ catalyst [8]. Supercritical carbon dioxide ($scCO_2$) also has unique properties as a solvent (Figure 3). $scCO_2$ is non-toxic and, after the reaction, separates easily by returning to the gas phase. In hydrogenation reactions, high yields can be achieved in a supercritical CO_2 medium [14].

Photocatalysis utilizes solar energy. Using a TiO_2 catalyst, organic pollutants can be degraded or synthetic reactions can be performed [13]. This method significantly improves energy efficiency [11]. Mechanochemistry conducts reactions through mechanical energy in ball mills. Solvent-free synthesis is possible, as in the case of the Knoevenagel condensation [8].

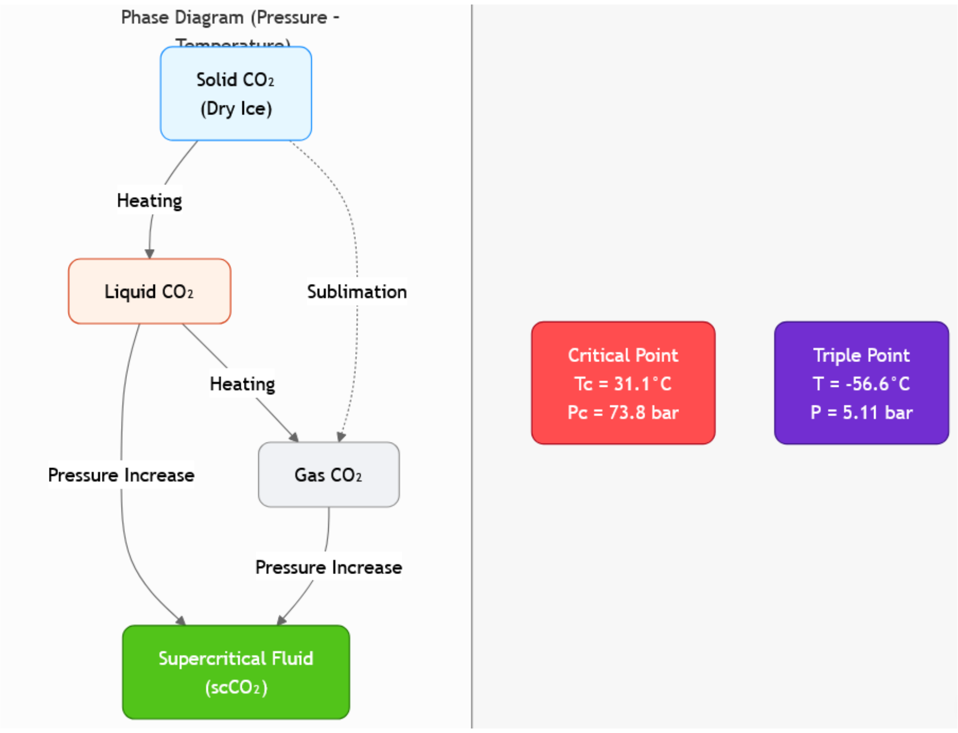

Figure 3. Phase Diagram of Carbon Dioxide (CO_2).

The supercritical fluid ($scCO_2$) forms above the critical point (Tc = 31.1°C, Pc = 73.8 bar) (Table 1). In this phase, CO_2 exhibits both gas-like diffusivity and liquid-like solvating power. In green synthesis, $scCO_2$ serves as a safe, recyclable, and non-toxic solvent [14,15].

Table 1. Critical parameters.

Property	**Value**	**Description**
Critical temperature (Tc)	31.1°C	No gas-liquid transition above this temperature
Critical pressure (Pc)	73.8 bar (7.38 MPa)	Minimum pressure for supercritical phase
Critical density	$468\ kg/m^3$	Gas and liquid densities equalize
Triple point	-56.6°C, 5.11 bar	Solid, liquid, and gas coexist

These methods can also be combined to create even more efficient processes. For example, peptide synthesis can be accelerated through the combination of microwave irradiation and biocatalysis [16].

RESULTS AND DISCUSSION

One practical example is the synthesis of ibuprofen. The traditional method consists of six steps and generates a large amount of waste, whereas the green route achieves an atom economy of up to 99% and requires only three steps (Figure 4). Catalytic hydrogenation and renewable feedstocks are employed in this process [18, 9].

Another example is the synthesis of aspirin (Figure 5). Using a microwave-assisted method, the reaction between salicylic acid and acetic anhydride is completed in 5 minutes with a yield of about 90% [7]. In water-based synthesis, penicillin production is carried out using enzymes, which significantly reduces energy consumption [16].

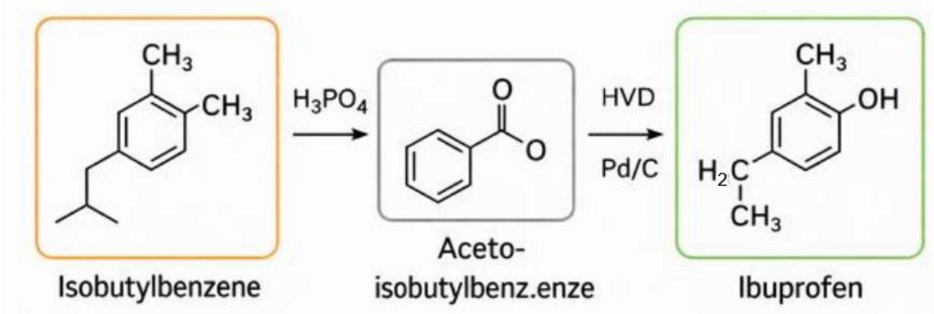

Figure 4. Three-Step Green Chemistry–Based Synthesis of Ibuprofen

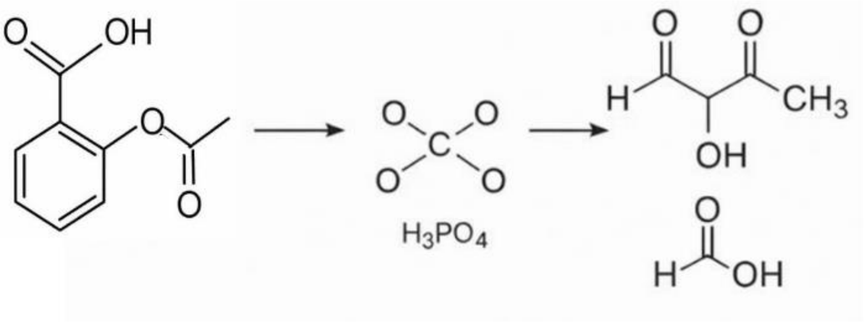

Figure 5. Synthesis Diagram of Aspirin with Structural Formula.

By applying green chemistry principles, Pfizer has reduced solvent usage in the synthesis of sertraline by 70% [6]. Bayer has optimized pesticide synthesis through biocatalysis [18]. At the laboratory scale, click chemistry—specifically the azide–alkyne cycloaddition—enables the safe and rapid synthesis of biomolecules [14].

These examples demonstrate that green methods are successful in both academic and industrial applications. In the future, the integration of nanotechnology and artificial intelligence will further enhance the optimization of green synthesis processes [10].

CONCLUSION

The expansion of green chemistry principles in organic synthesis represents an effective scientific approach to mitigating global environmental challenges—including climate change, resource scarcity, industrial waste, and the spread of toxic substances. The integration of nanotechnology, artificial intelligence, and automated synthesis systems will further enhance green synthesis processes in the future, providing substantial contributions to the sustainable development of the chemical industry.

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