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PRINCIPLE AND ROLE OF GREEN CHEMISTRY IN VARIOUS ORGANIC SYNTHESIS

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ABSTRACT

Green chemistry has shown over the past ten years how basic scientific methods can save the environment and human health while still being profitable. Significant advancements are being achieved in a number of important scientific fields, including catalysis, the creation of safer chemicals and solvents, and the growth of renewable feedstocks. Globally, industrial management, governmental policy, educational practice, and technology development all make extensive use of green chemistry principles (GCP). An overview of the 12 Green Chemistry principles' applicability is provided in this article. Within the broader framework of efficiency in organic synthesis, the essential ideas underlying the principles of green and sustainable chemistry are presented. The sustainability of their world is a subject that interests a lot of students today. They have a special chance to get in on the ground floor of the fascinating and rapidly developing field of green chemistry because they are chemistry students. Resources and educational materials linked to green chemistry are also covered. In this review, numerous green chemistry applications are examined. Green chemistry has significantly improved the sustainability factor of industrial processes, and it indicates the steps that should be made to develop and popularize green synthesis techniques.

Key words: Green Chemistry, Principles, Application, Education Resources.

INTRODUCTION

In the past, all of society's material necessities were met by Mother Nature.The advancement of modern chemistry has allowed us to change our natural resources and produce new matter from old for the good of society, which has tremendously improved our standard of living today. The heroic imagination, innovation, and creativity of chemists have affected every aspect of our daily lives, from the vibrant clothing we wear to the constantly evolving electronic products we "play" with, from the pharmaceutical agents to combat life-threatening diseases to the synthetic fertilizers to boost crop production for the needs of the world, from the rapidly expanding number of skyscrapers to the constantly accelerating speed of transportation.[1] The application of chemistry to reduce pollution is known as "green chemistry." It is more particularly the creation of chemical goods and procedures that are safe for the environment. The term "green chemistry" refers to all facets and varieties of chemical processes that lessen risks to both human health and the environment. Green chemistry links the design of chemical goods and processes with their effects on public health and the environment, and at its finest is ecologically friendly.[2]

After the Pollution Prevention Act of 1990 was passed, the focus on green chemistry in the US really took off. The Office of Pollution Prevention and Toxics (OPPT) was formed by the U.S. Environmental Protection Agency to investigate the possibility of creating new or upgrading already-existing chemical goods and processes to make them less hazardous to human health and the environment. A research initiative called "Alternative Synthetic Pathways for Pollution Prevention" was started by the office. This initiative offered previously unheard-of funds for studies involving the creation and synthesis of compounds that reduce pollution.[3] It is impossible to overstate the value of green chemistry as an option in the developing countries. Providing goods and services for a growing population without compromising environmental quality is essential to sustainable development. According to UN estimates, the world's population could reach 10.7 billion by 2050, and this population roughly doubling will result in a significant demand for chemical products and services.[4] Due to population expansion, the developing world is projected to experience a large portion of the chemical industry's growth. However, a lot of the environmental effects on the world linked to this population growth are linked to chemical methods or goods:

- Ozone depletion.
- Downstream pollution from unsustainable agricultural practices.
- Pollution of fresh and marine waters, further depleting food sources.
- Introduction of persistent organic pollutants into the ecosystem; loss of biological species in forests and waters.
- Introducing persistent organic pollutants into the ecosystem; and changing climate, causing as yet unpredictable changes in the hydrologic cycle with manifestations in flood, drought, sea-level change, and the spread of infectious diseases.

The idea of "green chemistry" is based on twelve principles that aim to reduce or remove harmful materials from the synthesis, production, and application of chemical products. As a result, there should be less or no use of materials that are harmful to human health and the environment. In the early 1990s, the idea of "green chemistry" was initially developed. The well-known green chemistry journal of the Royal Society of Chemistry published its inaugural volume in 1999, and the green chemistry institute was created in 1997. The twelve green chemistry principles serve as design concepts that assist chemists in reaching the deliberate objective of sustainability. Careful planning of chemical synthesis and molecular design to minimize unfavorable effects is the hallmark of green chemistry. One can establish synergy through appropriate design as opposed to just trade-offs. They exclusively use chemical products and chemical methods that do not harm the environment. It is based on creating molecules, reactions, materials, and processes from scratch that are safer for the environment and for human health. Nearly all branches of chemistry, including inorganic, organic, biochemistry, polymer, environmental, and toxicological, are involved in green chemistry processes.[5] The objectives of environmental protection and financial gain can be achieved through a number of popular trends in the green program, such as catalysis, bio-catalysis, and the use of safe alternatives, such as renewable feedstock (biomass), reaction solution (such as water, ionic liquids, and supercritical liquids), reaction conditions (microwave irradiation), and new synthetic pathways (photocatalytic reaction).[6]

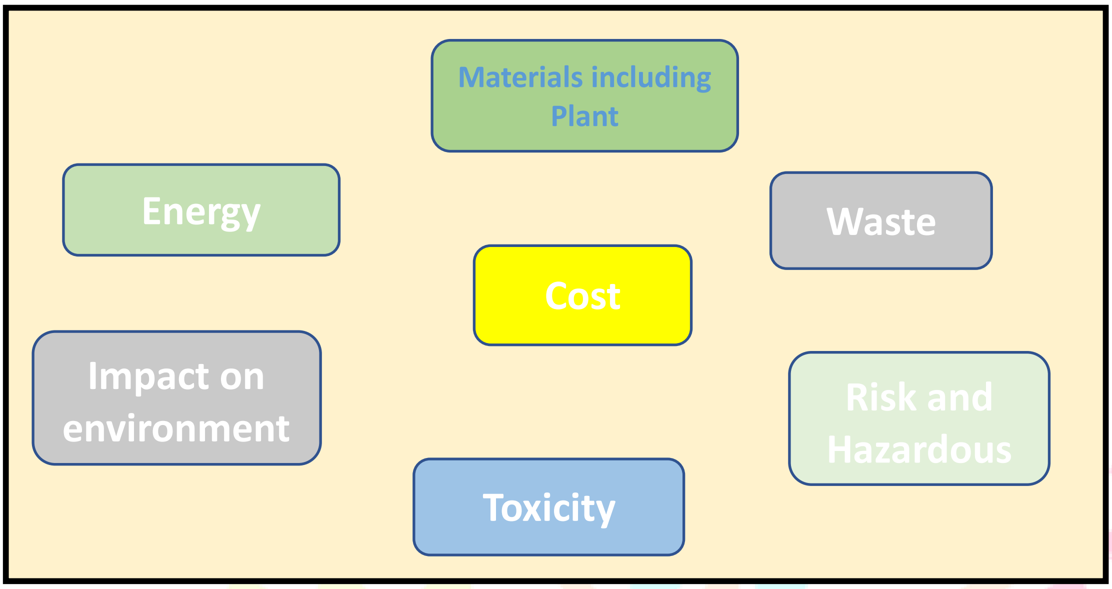


Figure 1. Green chemistry reduce

The idea of design is the key component of green chemistry. Design cannot be done by accident because it is a statement of human intention. It includes innovation, preparation, and methodical conception. The Twelve Principles of Green Chemistry are "design rules" that can be used by chemists to help them attain the deliberate objective of sustainability. Careful planning of chemical synthesis and molecular design to minimize unfavorable effects is a hallmark of green chemistry.[7] One can achieve synergy through appropriate design—not just trade-offs. The goal of the Green Chemistry method is to establish molecular sustainability. It is hardly unexpected that it has been used in various industry areas given this objective. There are countless examples of successful uses of honorable, commercially viable technology in industries as diverse as agriculture, automotive, cosmetic, electronics, energy, household goods, and pharmaceuticals.[8]

The rise and fall of Easter Island, which the Polynesians discovered approximately 400 AD, is a striking example of how a community can lose its viability. Its population peaked at likely more than 10,000, considerably surpassing what the neighbourhood ecosystem could support. From 1400 to 1600, the woodlands were cleared for farming and for the transportation of the enormous stone monoliths, or "Moai". Deforestation, soil loss, and erosion have all been found in the island's core samples, and these factors have contributed to overpopulation, food shortages, and ultimately the collapse of the community. The history of Easter Island thus demonstrates that the survival of our civilization rests on our ability to simultaneously provide the world's rapidly expanding population with enough energy, food, and chemicals without endangering the planet's long-term health.[9]

In order to make sure that our next generation of chemicals, materials, and energy is more sustainable than the one we have now, chemistry plays a crucial role. The creation of new and affordable methods for pollution control is necessary given the global need for chemical processes and products that are ecologically benign.

Green Chemistry, which refers to the application of a set of principles that lowers or eliminates the use or generation of hazardous compounds in the design, manufacture, and applications of chemical products, is one of the most alluring ideas in chemistry for sustainability. Even if some of the concepts seem to be basic sense, using them all together as a framework for designers usually necessitates redesigning chemical goods or procedures. It should be noted that the rapid development of Green Chemistry is due to the recognition that environmentally friendly products and processes will be economical on a long term.[10] This paper examines numerous instances where green chemistry has improved sustainability and makes recommendations for the actions that should be made to support and popularize green synthesis processes.[11]

The principles of green chemistry are the focus of research programs and centers across the Americas, Europe, Asia/Pacific, and Africa. This research has a very broad scope and covers topics including polymers, solvents, catalysis, biobased/renewable materials, technique development for analytical and synthetic processes, and the creation of safer chemicals. Each of these fields has excellent research being done that aims to incorporate one or more of the 12 Principles of Green Chemistry.[12]

The Green Chemistry Framework

The three key components of the Green Chemistry framework are as follows:

1. Green Chemistry plans take into account the entire chemical life-cycle.
2. Green chemistry aims to eliminate the inherent risk of chemical products and processes by designing them from the ground up.
3. Green Chemistry functions as a system of guiding principles or design standards.[13]

GREEN CHEMISTRY PRINCIPLES.

Paul Anastas and John Warner introduced the twelve tenets of green chemistry in 1998. These principles serve as a foundation for the design of new chemical products and processes, and they relate to all facets of the process life-cycle, including the raw materials used, the effectiveness and safety of the transformation, the toxicity and biodegradability of the products and reagents used. Recently, they had a constructive briefing on the more appropriate and memorable acronym.[14]

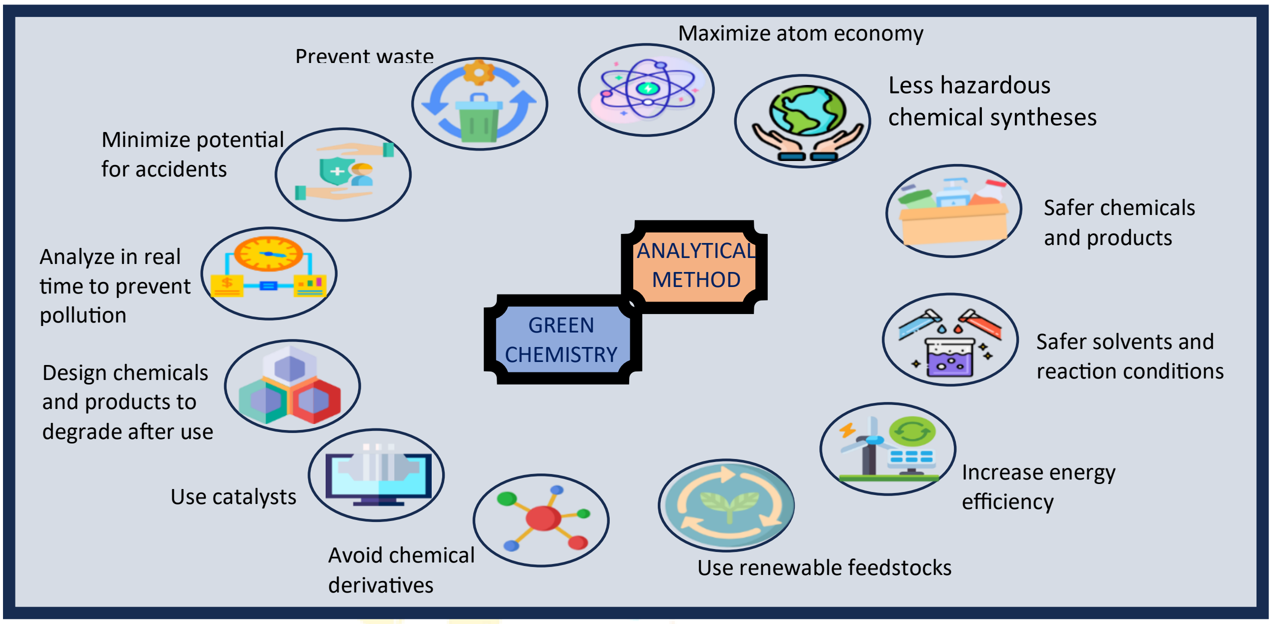


Figure 2: Green chemistry principle's

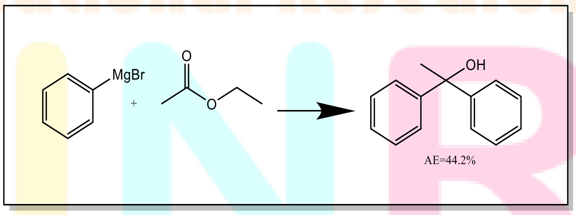
MAXIMIZE ATOMIC ECONOMY

Atom economics (AE), also known as atom efficiency, was first developed by Barry Trost in 1990 and relates to the idea of maximizing the utilization of basic materials. For instance, the maximum number of atoms from the reactants are present in the final product. All the atoms from the reactants would be included in the ideal reaction. The molecular weight of the desired product divided by the molecular weights of all the reactants utilized in the reaction is used to calculate the AE (Figure 3). It is an abstract value designed to quickly determine how effective a reaction will be[15]

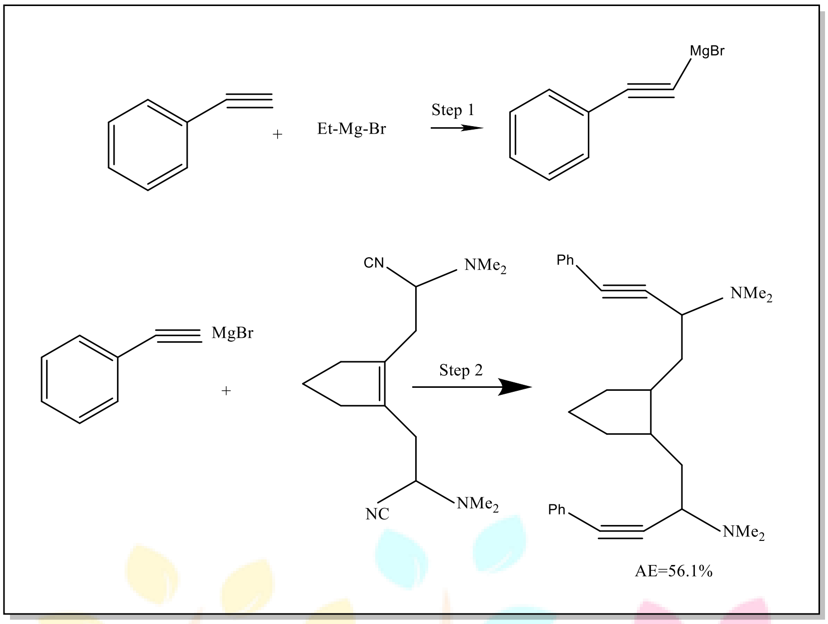
The Atom Economy AE

AE= MW of Product /MW of reagents

Example of a Grignard reaction



Applications to the synthesis of propargylic amine



Diels Alder reaction

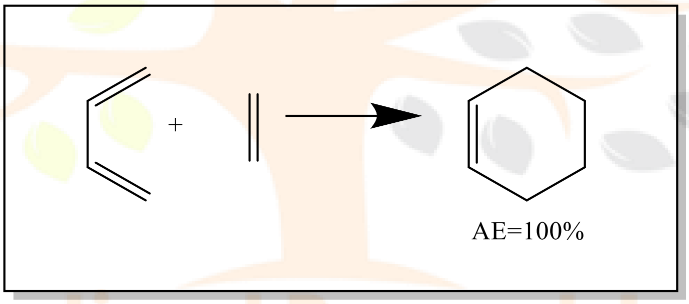
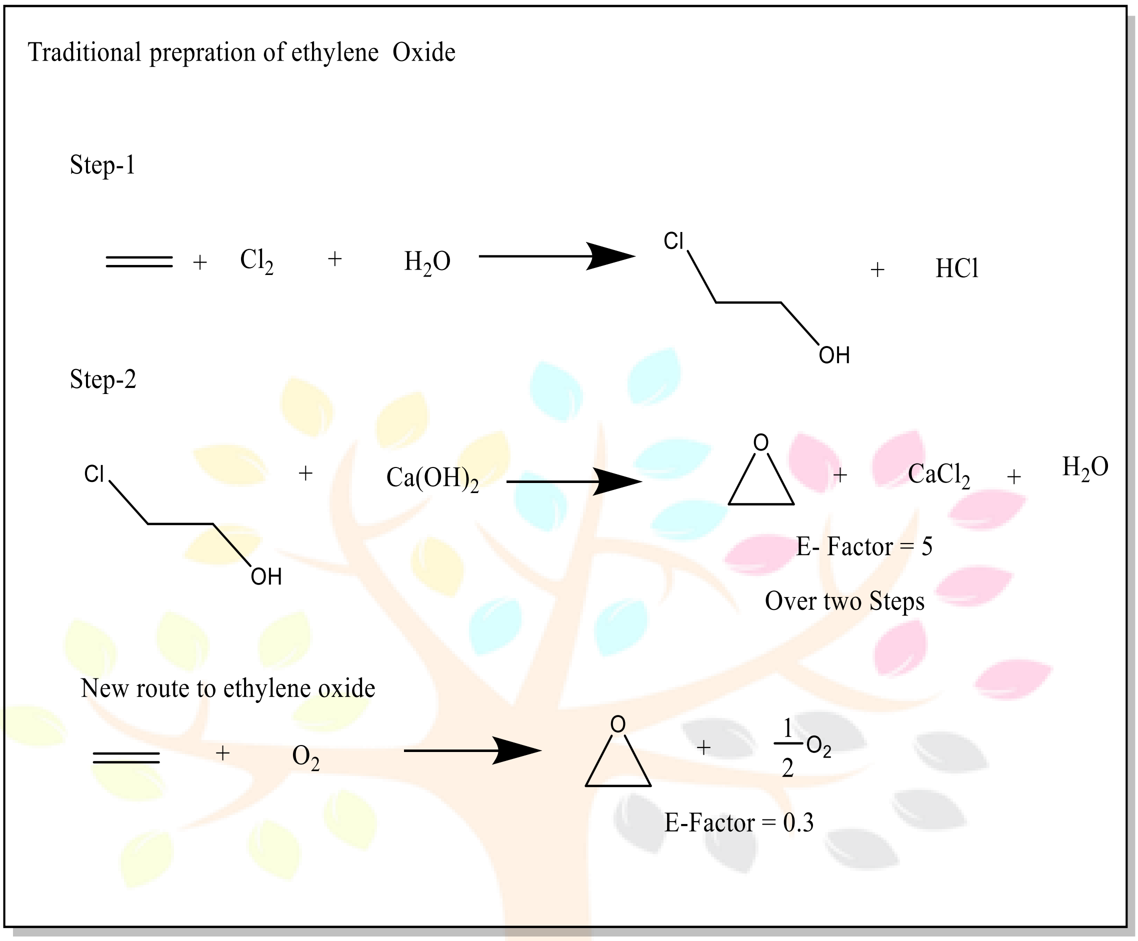


Figure 4. The atom economy AE and several demonstrations.

Prevent Waste

Avoiding waste formation is preferable to cleaning up after it has already occurred. Waste can be defined as the creation of any material with unrealized worth or the loss of energy that is not put to use. As was already established, garbage can come in a variety of shapes and sizes, and its type, toxicity, quantity, and method of release can all have an impact on how it interacts with the environment.[16] A process will unavoidably produce waste, which is by definition unwanted, if significant amounts of the initial raw materials employed in the process are lost due to the process's original design. Roger Sheldon first proposed the idea of what is now often referred to as the E-Factor, or Environmental Impact Factor, in 1992.[17] This measure aids in calculating the waste produced per kilogram of product. It is a way to judge if a manufacturing process is "environmentally acceptable." The environmental concern, which is now widely accepted in the chemical sector, highlights how ineffective some industrial methods have been and makes way for original solutions. The early synthesis of ethylene oxide, which was made via a chlorohydrin intermediate (Fig. 4a), is one such example. As shown earlier, the whole synthesis's E-Factor.[18] Five kilograms of garbage were to be disposed of for every kilogram of produce. This does not account for the waste water that has been tainted with chlorine by products. The E-Factor decreased to 0.3 Kg of waste when the synthesis was changed to use molecular oxygen, eliminating the need for chlorine.



(a)

(b) Revalorization of biofuel by products

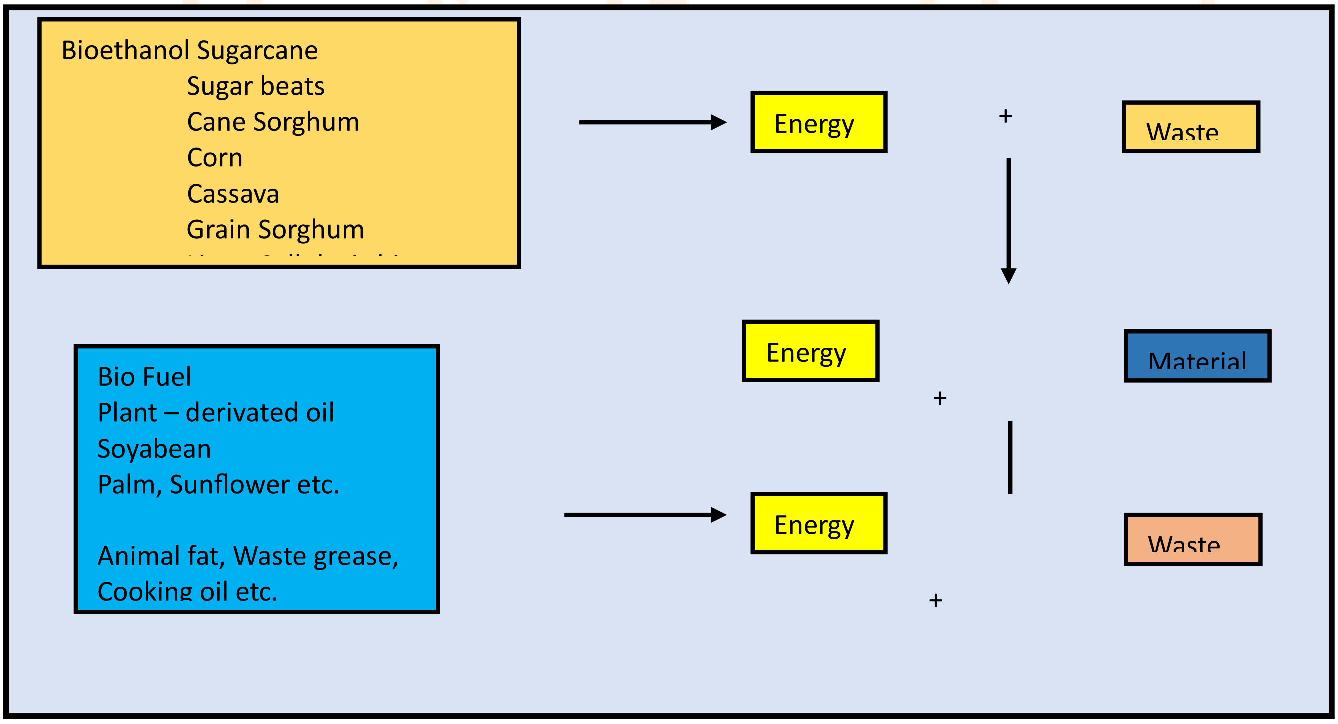


Figure. 5(a) Traditional preparation of ethylene oxide and the new route relying on molecular oxygen. (b) revalorization of biofuel by products.

The creation of waste water was also prevented by the new procedure, which produced more than 16 times less trash than the old one. When byproducts are unavoidable, creative alternatives should be investigated. One effective option is to pursue an industrial ecology strategy, in which waste can be transformed back into a new raw material with substantial value as it enters the life cycle. Currently, this strategy is being used to produce biofuel.[19] (Fig. 5b).

Less Hazardous Chemical Synthesis

The more recent green reactions that have emerged during the last ten years have supplemented some of the earlier ones. Rearrangement cycloaddition- or multi-component coupling-based reactions are two examples of effective reactions that have long been known to exist. An excellent illustration of the cleaner, more efficient synthetic tools available to organic chemists is the use of enzyme reactions, C-H activation, cascade or tandem reactions.

Biological enzymes can substitute hazardous chemicals in many industrial processes, making them more efficient and less expensive.[20] For instance, the concept of a revolutionary polycarbamate synthesis (PC) method that uses CO_2 instead of hazardous carbonyl dichloride ($COCl_2$) is simple. This method also results in the removal of the solvent dichloromethane (CH_2Cl_2). Ethylene oxide $(CH_2)_2O$, carbon dioxide (CO_2), and bisphenol-A ($Cl_5H_{16}O_2$) are all involved in the reaction, which results in polycarbamate and ethylene glycol ($C_2H_6O_2$) as illustrated below.[21]

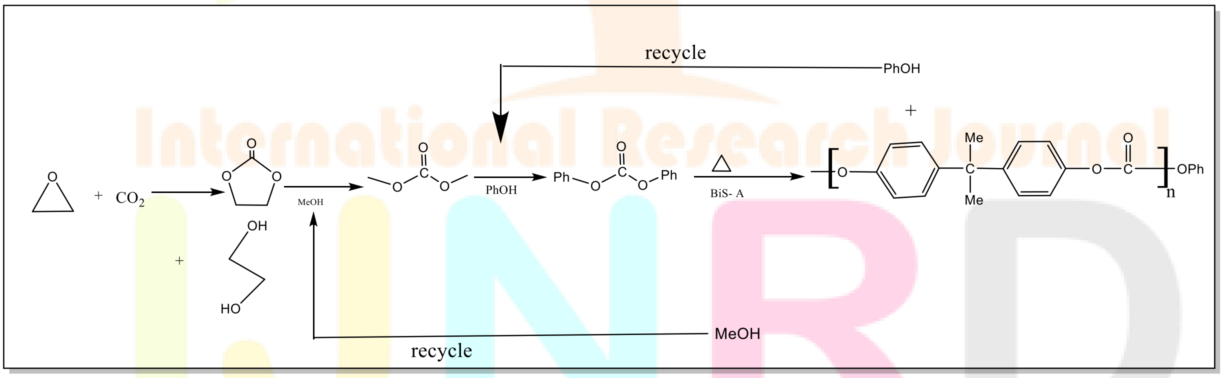


Figure.6 Synthesis of polycarbamate

DESIGN CHEMICAL AND PRODUCTS TO DEGRADE AFTER USE.

Although there has been a lot of attention paid to creating chemicals for a variety of uses, from medicines to materials, there has been a startling lack of focus on taking danger into account during the design process. Sustainability requires an understanding of the characteristics of molecules that affect the environment and the changes that occur in the biosphere. Chemistry will be able to legitimately build molecules that are safer for people and the environment once it has mastered this understanding. Work by Garrett and Devito in 1996 and Ariens in 1984 demonstrated that creating safer compounds is not only essential for the growth of green chemistry but is also feasible. A substantial amount of work has been done in the field of toxicology in recent decades to transform it from a descriptive science to one with a significant mechanistic component, and more recently, progressively towards the introduction of an in-silico component.[22] This transformation has made it possible to link structure, properties, and function through correlations, equations, and models. These methods serve as the cornerstone for the efforts being made to create a thorough design plan. For instance, by incorporating certain design elements that prevent their entry into humans and many animal creatures, the existing knowledge of medicinal chemistry can already assist define some guidelines for producing less harmful compounds.[23]

SAFE SOLVENTS

Wherever possible, it should be unnecessary and harmless to utilize compounds like solvents and separating agents. For instance, solvents, which are major sources of environmental pollution, were employed in enormous quantities during chromatographic separations. The majority of conventional organic solvents are poisonous, flammable, and corrosive.[24] Their recycling is linked to a distillation process that uses little energy but suffers significant losses. Therefore, it is necessary to produce solvents that are beneficial to the environment. The use of auxiliary chemical substances should be avoided wherever feasible, according to safer solvents, and if they must be used, they should be harmless. The selection of viable substitutes for organic solvents is based on process safety, worker safety, environmental safety, and process sustainability, in accordance with the tenets of green chemistry.[25] The solvent should be low volatility, physically and chemically stable, simple to use, and simple to recycle. The most active field of green chemistry research may be solvents. They represent a significant obstacle for green chemistry since they frequently make up the large majority of mass lost during synthesis and processing. Several common solvents are also poisonous, flammable, and corrosive. Their volatility and solubility have raised the risk of worker exposure and resulted in catastrophic accidents by causing pollution of the air, water, and land. When possible, recovery and reuse involve energy-intensive distillation and occasionally cross-contamination.[26] Chemists began looking for safer alternatives to meet all of these drawbacks. Some of these novel "green" solutions include solventless systems, water, supercritical fluids (SCF), and more recently, ionic liquids. The ideal condition would be to avoid using any solvent whenever possible because choosing to add an auxiliary always entails work and energy to remove it from a defined system. As a result, efforts have been made to create systems without solvents. The observation that solvents account for the majority of industrial waste served to support this notion. Additionally, depending on the physical characteristics of the reagents used or the desired transformational consequence, the method frequently requires new or revised chemistry to enable the reaction to continue without the initial solvent.[27]

The most prevalent molecule on the earth is water, which is also occasionally referred to as a safe universal solvent. Therefore, there are significant benefits to being able to conduct a reaction in water. As is well known, water is risk-free and safe, making it an advantageous solvent for large-scale chemical reactions.

Because many organic molecules do not dissolve in water, the characteristics of water have even increased reaction speeds through the hydrophobic effect and made separation easier. One of the helpful examples illustrating the benefits of using water as a solvent is the instance of an enhanced Diels-Alder process in water.[27] One drawback that could impede industrial applications and which has not yet been addressed is the potential for water pollution, which can be difficult to clean.[28]

INCREASE ENERGY EFFICIENCY

The development of more energy-efficient processes and the hunt for renewable energies—non-depleting resources in a time frame relevant to human scale—have been driven by growing worries over the depletion of petroleum feedstocks and the increase in energy demand. Unused energy can be regarded as a waste, as was said in the first part (first principle). It is highly desirable to develop chemical processes or systems that don't consume a lot of energy. One example of what chemists can do to reduce energetic requirements is to lower the energy barrier of a chemical reaction or select suitable reactants so that the transformation can happen at ambient temperature, with all the direct and indirect benefits associated with it.[29] Increasing a chemical system's energy efficiency is just one aspect of the answer. Alternative forms of energy are also required. Biofuel production, solar power (thermal and photovoltaic), wind power, hydro power, geothermal energy, and hydrogen fuel cells are a few examples of these sustainable energies.[17] Green chemists, who are skilled at creating materials or chemical systems that may be used to gather part of those renewable natural energies, once again have a crucial role to play in addressing this new challenge. One of the substitutes for petroleum is solar energy, which is currently the world's main sustainable energy source. It has taken a lot of work to comprehend and develop chemical systems that can transform solar radiation into voltaic energy.[30] Although interest has been shown in organic, inorganic, and hybrid solar cells, organic solar cells have attracted the most attention due to their higher efficiency. The ability of the material employed to absorb photonic energy from solar radiations is the foundation of such cells. As a result of the absorption, excited states are created that can be relayed and produce electrical current. The development of materials and polymers that effectively convert light into current is still a difficult task, but it is essential to the success of this strategy. Another possibility for addressing the impending rise in energy demand is the use of proton exchange membrane (PEM) fuel cells that run on hydrogen and oxygen gases (Fig. 7).Particularly in the last ten years, with the creation of increasingly effective catalysts like nanoparticles or even hydrogenase enzymes, PEM fuel cells have attracted study attention.[31] The risk of handling hydrogen gas, which is very volatile and explosive, is a key factor in this method.

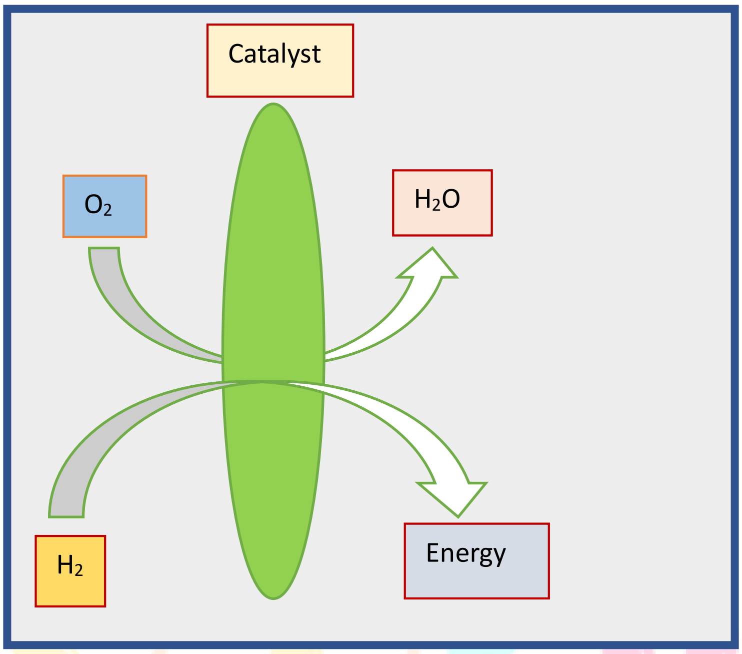


Figure.7 General concept of hydrogen fuel cell

REDUCE DERIVATIVES

Because these processes require additional reagents and produce waste, unnecessary derivatization such as blocking groups, temporary change of physical or chemical processes, and protection/deprotection should be minimized or avoided.[15] If at all possible, biological synthesis ought to be employed developed a non-covalent protective group between bis-(N,N-dialkyl)terephthalamides and hydroquinones in the form of a co-crystal (Fig. 8), where this method was practical and effective for the industrial process. It eliminated the issue without changing the original hydroquinone structures and decreased energy and waste.[23]

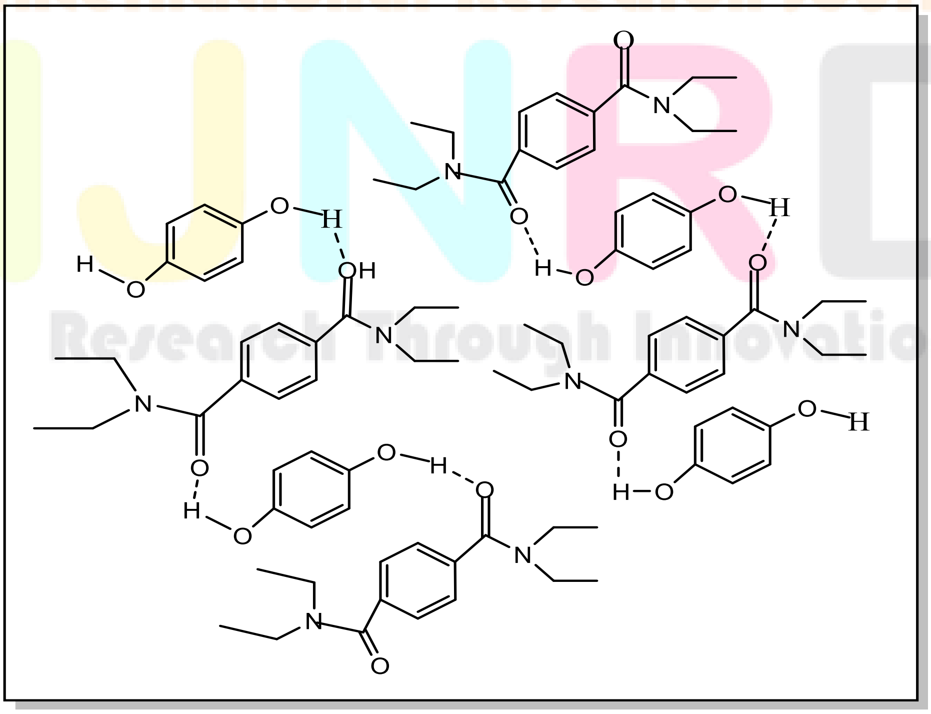


Figure.8 Illustrates 8 hydroquinones protected by non-covalent interactions with bis (*n*, *n*-dialkyl) terephthalamides

RENEWABLE RESOURCES

According to estimates, the great majority of our manufactured goods come from natural gas or petroleum feedstock. Numerous facets of our consumer culture and economy will be impacted as a result of the depletion of those resources. It is now more important than ever to switch to renewable feedstocks for both fuel and building materials[32]. Biomass, or the material derived from living beings, is the primary renewable feedstock on the planet for both material and energy. This comprises food, agricultural waste, wood, and other materials. cellulose, lignin, suberin, and other wood components, as well as polyhydroxyalkanoates, lactic acid, chitin, starch, glycerol, and oil, are examples of renewable materials. For instance, lignin is a significant waste product of the pulp and paper sector. It has long been used as fuel for burning at the industrial site. It has discovered new uses recently, such as dispersants, additives, and raw materials for the manufacture of compounds like vanillin, DMSO, or humic acid.[33] Another common natural polymer that makes up the exoskeleton of arthropods (like crustaceans) is chitin. It is a significant by product of the seafood industry and can be deacetylated to become chitosan.[25] Chitosan has been used for a wide range of industrial purposes, including water filtration and biomedical applications.[34] It should be possible to replace the current petroleum feedstocks with a significant amount of raw materials by recycling this bioindustrial waste.[34]

CATALYSIS

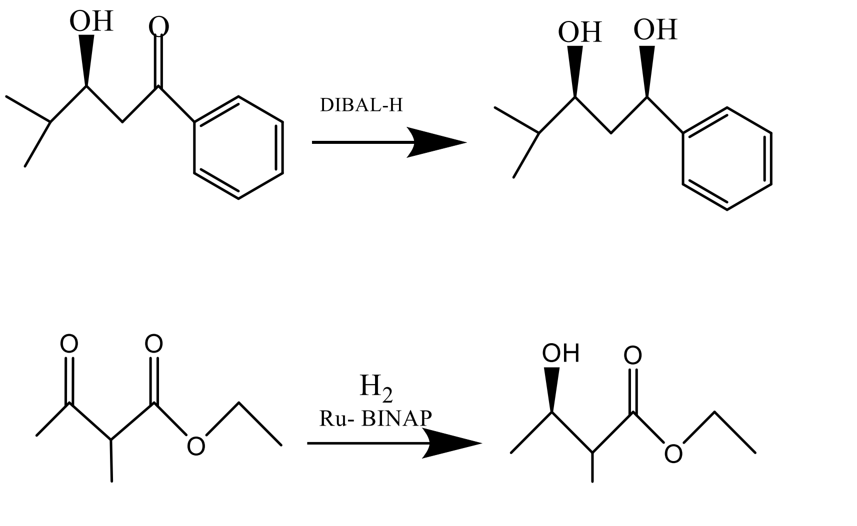
Stoichiometric reagents are inferior than catalytic reagents. As is well known, using a stoichiometric amount of reagents traditionally results in the generation of waste in many situations.[25] The catalysis principle promotes the use of biodegradable catalysts for environmental preservation since they require less energy, avoid using organochlorine compounds, and utilize less waste water and energy.[35]

In addition, bio-catalysis, a biomimetic strategy based on natural or altered enzymes, provides an illustration of green chemistry. It often denotes both the usage of pure enzymes directly and the changes carried out by designed biological things. Additionally, the mild reaction conditions allow for the transition to occur in water at air pressure and room temperature. Enzymes have also shown to have higher chemical selectivity and stereochemistry.[35]

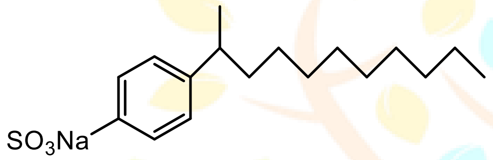
Additionally, biocatalysts offer a significant advantage over non-biological catalysts in terms of reaction rate, cost, catalytic specificity, etc., but lack heat sensitivity and have poor durability.[36]

BIODEGRADATION

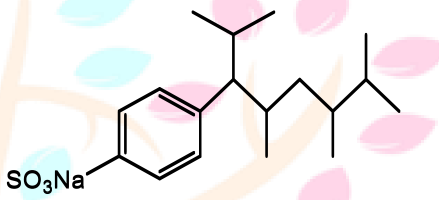
Long recognized, the persistence issue first surfaced during the infancy of the industrial revolution[4]. For instance, tetrapropylene alkylbenzene sulfonate (TPPS) accumulated in the water supply during the 1950s due to an incomplete breakdown when it was utilized as a surfactant for laundry detergents.[8]



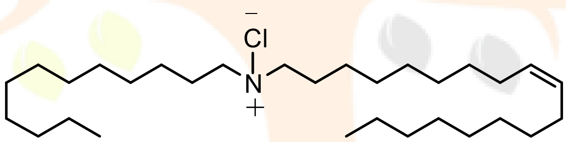
Comparison between Stochiometric and Catalytic Reduction



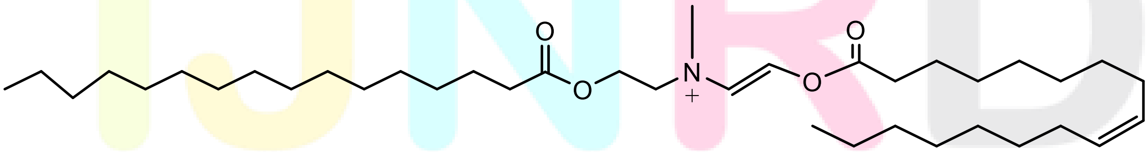
Linear alkyl benzene Sulfonate
LAS



Tetrapropylene benzene sulfonate
TPPS



Di(hydrogenated)tallowdimethyl ammonium chloride(DHTDMAC)
Biodegradability Factor- 0.5 %



Di(ethyl ester) dimethyl ammonium chloride(DEEDMAC)- Biodegradability Test- 76%

Figure.9 Integrating biodegradability in the design of surfactants

There were times when the situation was so dire that "water tended to foam when coming out of the tap." The industry looked for a quick fix in response to the public outrage and discovered that changing the methyl branched chain of TPPS to a linear carbon chain decreased biopersistence (Fig. 9). The replacement of linear alkylbenzene sulfonate (LAS) with TPPS is a typical example.[25] The persistent problems with environmental contamination act as a reminder of how challenging it is to develop biodegradable substances. Several decades of data collection have revealed tendencies. Chemical structures such halogenated moieties, branching chains, quaternary carbons, tertiary amines, and specific heterocycles should be avoided since they might have greater persistence. On the other hand, including functional groups like esters or amides that are recognized by common enzymes could aid in the creation of products that are environmentally friendly.[25,37] Surface-active quaternary ammonium compounds that are utilized as domestic fabric softeners were the subject of this approach.[37] Long chain ammonium salts were released into the environment up to the 1990s, including di(hydrogenated)tallow dimethyl ammonium chloride (DHTDMAC). It was later found that their inherent ecotoxicity was high and their rate of biodegradation in aqueous sediment was poor. Hydrolyzable amide or ester bonds were developed in response. The new ammonium salts have demonstrated to be more biodegradable; di(ethyl-ester) dimethyl ammonium chloride (DEEDMAC) replaced DHTDMAC, and this was followed by a 70% increase in the biodegradability.[37]

ANALYSIS

The use of analytical techniques that generate less waste and are safer for the environment and human health is known as "green analytical chemistry".[17] This concept takes into account both the environmental drawbacks of conventional analysis and the live monitoring of a chemical change. Analytical chemistry that produces no waste aims to measure compounds. Analytical chemistry-related environmental issues are frequently connected to the analytical procedure.[3] Analytical apparatus manufacturing materials should be taken into account. When developing novel sensors, green chemists and engineers must be conscious of the material's toxicity as well as any potential environmental issues. For instance, electrochemistry frequently use mercury electrodes. By substituting them with carbon-based electrodes such nanotubes or nanofibers, the practical solution has been demonstrated.[38]

ACCIDENT PREVENTION

The number of hazardous materials and procedures has increased in our workplace. The "Chemical accident prevention and the clean air act amendments of 1990" state that identifying and evaluating the hazards is the first step in preventing accidents.[25] Toxicological, physical, such as flammability or explosivity, and global risks should all be taken into consideration when developing new chemicals and manufacturing techniques to avoid mishaps like the Love Canal or Bhopal.[8,25] The UCLA catastrophe that took place in January 2009 serves as a stunning and current example of these risks.[25] Unfortunately, improper handling of the widely used and highly combustible butyllithium reagent led to the research assistant's tragic death. The scientific community should take this disaster as a powerful wake-up call that many of the chemicals we still use pose serious risks and should be replaced with safer alternatives to minimize the risk of mishaps.[39]

PHARMACEUTICAL PERSPECTIVE

Green chemistry concepts demonstrably increase economic and environmental performance when applied to a pharmaceutical paradigm. For individuals prepared to take on the additional priorities of Green Chemistry, this is accompanied by success and personal growth.[6] Continuous re-examination and questioning will certainly result in increased scientific excellence, and the achievement of greater efficiency will finally provide a competitive edge. There are numerous instances of Green Chemistry concepts being successfully used in discovery, including the use of microwave chemistry, supercritical separations, and high-throughput screening, which can produce drug candidates with less waste and in less time.[40] And yet, authoritative overviews describing the future of medicinal chemistry do little more than mention the term Green Chemistry. The challenge for each scientist in discovery is to apply Green Chemistry principles to address their own list of immediate priorities for higher efficiency. Pharmaceutical Green Chemistry begins in discovery, and the medicinal scientists who successfully incorporate Green Chemistry principles are the innovators leading the way to more productive medicinal chemistry.[7]

APPLICATIONS OF GREEN CHEMISTRY IN SOME ORGANIC REACTIONS

1. ALCOHOL ACTIVATION FOR NUCLEOPHILIC SUBSTITUTION

Active pharmaceutical ingredients (APIs) are routinely prepared using the substitution of activated alcohols. According to a recent study, 64% of all nitrogen substitution reactions were alkylations, while 2% of transformations involved turning alcohols into halides or sulfonate esters (always for additional use).[41] Although it should produce water as a byproduct, direct nucleophilic substitution of an alcohol is appealing since hydroxide is a poor leaving group that typically needs activation. Through an SN1 reaction, it is possible to substitute some allylic, benzylic, and tertiary alcohols directly, although this method often calls for too much Bronested or stoichiometric Lewis acid and lacks control over stereochemistry.[41] Using a Mitsunobu technique, secondary alcohols can be substituted with good stereospecificity; the difficulties with this protocol are covered below. Activation is inefficient because it necessitates further processing, the activating group must be removed from the product after it has been displaced, and the trash that results from these steps must be disposed of. The production of ropinirole 1(Fig.10), a dopamine agonist, serves as an example of the effects of activation.[41] Dipropylamine replaces the toluenesulfonate (2, R = OTs), resulting in an 85% yield of ropinirole. The net conversion of alcohol (4, R = OH) is accomplished in 74% yield, which represents a major improvement over an earlier approach where displacement of bromide (3, R = Br) generated ropinirole in 57% yield due to competitive elimination. A mass intensity of 25 kg was used in the manufacture of 2 from 4. Encouraging new developments have been made in this field.[41] Alkylic and benzylic alcohols can be catalytically activated using indium(III) chloride to be displaced by acetylenic, allylic, or propargylic silanes1 and they can also be catalytically activated using 4-toluenesulfonic acid, including polymer-bound acid, to be displaced by a variety of carbon, nitrogen, oxygen, and sulfur nucleophiles.

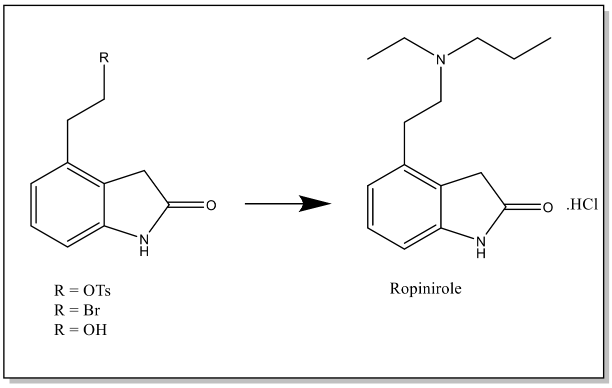


Figure.10 The synthesis of ropinirole

By in situ oxidation and reduction catalyzed by iridium complexes, amines have been replaced for a wider spectrum of alcohols, including primary and secondary alcohols. This method has been expanded to include the creation of carbon-carbon bonds, for instance utilizing a catalyst made of ruthenium.[42] It is still difficult to develop a secondary alcohol activation technique that keeps the reaction's stereochemistry under control.

2. ASYMMETRIC SYNTHESIS OF AMINES FROM PROCHIRAL KETONES

In recent years, academic and industrial researchers have investigated the production of a-chiral aliphatic amines from prochiral ketones. Reports of generic techniques with significant enantiomeric excess, however, are uncommon.[41] Indirect reductive amination techniques are frequently employed. The majority of these are restricted to particular situations, such as enamine hydrogenation, enantioselective alkylmetal addition to aliphatic aldimines, and enantioselective catalyzed by iridium complexes. This method has been expanded to include the creation of carbon-carbon bonds, for instance utilizing a catalyst made of ruthenium. It is still difficult to develop a secondary alcohol activation technique that keeps the reaction's stereochemistry under control.[43]

Ketimine derivatives can be transferred into hydrogen, chiral imines can be added diastereoselectively, or chiral methylbenzyl ketimine derivatives can be reduced diastereoselectively.[43] Racemic amines can be produced very effectively by the direct reductive amination of ketones, as demonstrated in Fig.11. However, it has been challenging to develop asymmetric versions of this response. It would be tremendously beneficial to have a universal method for producing a-chiral aliphatic amines directly from prochiral ketones in the chemical transformation toolkit.[44] The direct reductive amination of ketones could offer significant advantages in terms of overall efficiency and environmental effect, aside from the elimination of additional processes to produce and isolate the imine substrates.[45]

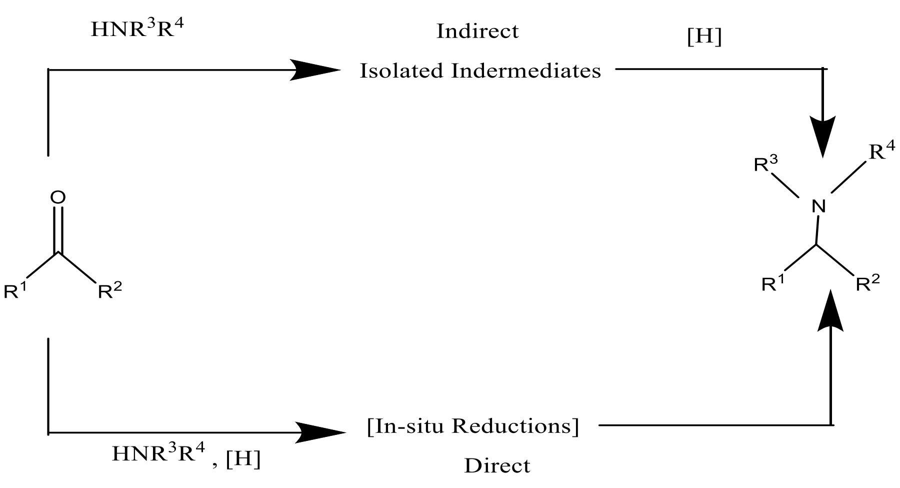


figure.11 assymetric synthesis of amines from prochiral ketones

3. NEW GREENER FLUORINATION METHODS

Fluorine has been employed more frequently to block metabolic sites or to modify the electronic properties of drug candidates without adding steric bulk because of its distinctive stereoelectronic capabilities.[44] 10% and 14%, respectively, of drugs that have been commercially released and therapeutic candidates that are now undergoing phase III clinical studies contain fluorine-containing compounds.[41]

Only the chemistry involved in creating the F-C bond appears to be a restriction on the possibilities for fluorine incorporation. There are just a few techniques for adding fluorine to target compounds, and the majority of them call for strong reaction conditions and the employment of dangerous and corrosive chemicals. As a result, chemists are restricted in their ability to investigate all structure-activity relationship (SAR) regions since they rely so heavily on starting materials that they have already added fluorine to. Three categories for fluorination are commonly used[46](Figure 11.1):

1. Fluorine exchange employing HF or its alkali/ammonium salt with a leaving group[41] (Cl, Br, I, OH, OSO2R, etc.).

2. Deoxyfluorination: turning an alcohol into an aliphatic fluoride (R1R2CHOH A R1R2CHF) or an aldehyde or ketone into a gemdifluromethylene (R1R2CLO A R1R2CF2). For this reason, DAST has long since supplanted the notorious SF4, and more recently, Deoxo-Fluor TM, a more reliable and user-friendly alternative, has appeared.[41]

3. Direct fluorination from an electrophilic (F+) source (e.g. Selectfluor TM).This usually requires a carbon nucleophile, such as the enolate of an aldehdye, ester or amide.[47]

Research on fluorination is quite active, and new agents are constantly being developed. One such agent is 2,2-difluoro-1,3-dimethylimidazoline (DFI), which exchanges a fluorine for a hydroxyl group.56 There is still a need for catalysts to increase the nucleophilicity of F2, softer conditions for fluorine exchange reactions (ArCl ArF), and safer and more affordable sources of electrophilic fluorine in the

field of adding fluorine to medicinal molecules.[48]

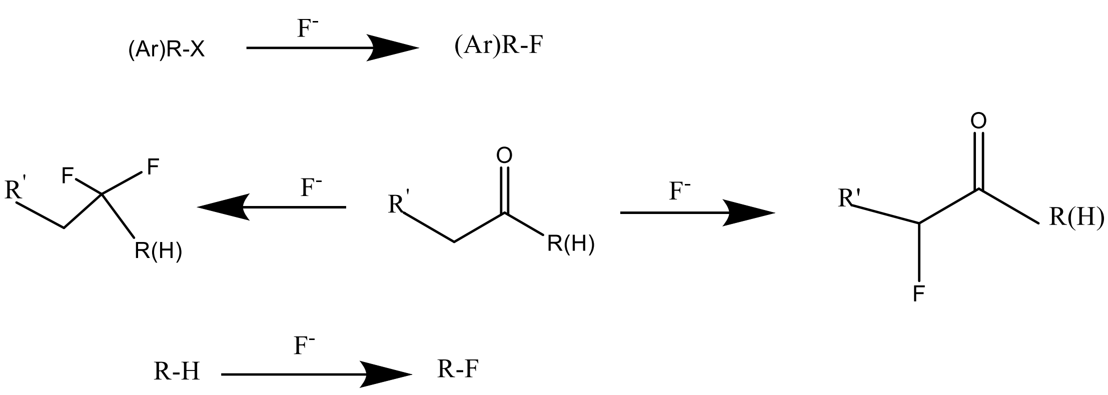


Figure. 11.1 Common methods to introduce flourine.

EDUCATIONAL MATERIALS AND RESOURCES

The creation of green chemistry curricular materials is one thing that is accelerating the integration of pollution avoidance into industrial manufacturing processes significantly. The chemical industry is learning that when their chemists are informed on principles in pollution-prevention, they are able to identify, develop, and put into practice methods that minimize pollution and costs. The ACS Division of Education and International Activities and EPA-OPPT collaborated to produce resources to give future generations of chemists the skills and knowledge to practice green chemistry. This was done to make it easier to integrate green chemistry into the classroom. These materials are primarily intended for undergraduate and graduate chemistry students, although they may also be of interest to professional chemists, K–12 students, and members of the general public.[49] Dedicated fellowships, scholarships, and research grants are additional essential educational resources that help to shape interest in green chemistry. These funding enable academic staff and students to give particular research activities their undivided attention. Similar to conferences, symposia, and workshops, attending them enables researchers, professors, and students to all develop a thorough understanding of green chemistry.

The ACS and GCI will support the CHEMRAWN XIV World Conference on Green Chemistry, "Toward Environmentally Benign Processes and Products," in collaboration with the International Union of Pure and Applied Chemistry (IUPAC).2 Leaders from academia, business, and government will attend the Conference, which will take place in Boulder, Colorado, from July 9–13, 2001. The goal is to design a strategy for sustainable development that strikes a balance between economic growth and environmental conservation by using upstream pollution prevention. Public attendance and a strong student program make CHEMRAWN XIV a valuable platform for networking and knowledge. Additionally, the GCI makes information available via a website and email list-server. 3The website offers details on GCI, links to sites with related material from the government, business, and academia, as well as information on Green Chemistry initiatives around the world. More than 300 people are connected through an email list-server, allowing for quick dissemination of information about job openings, upcoming conferences, and a place to ask subject-matter specialists questions.[50]

CONCLUSION

As stated earlier, the objective of "green chemistry" is to limit the amount of dangerous components used in the manufacture and use of chemical goods. It is well knowledge that it is impossible to simultaneously satisfy the needs of all twelve process principles when building a green chemical process. Nevertheless, it makes an effort to incorporate as many concepts as it can into some of the synthesis processes. There are numerous ways to meet green chemistry's objectives of economic growth and environmental conservation. Chemical goods, for instance, might be prepared to degrade into harmless byproducts rather than stay in the environment after serving their purpose. The primary purpose of green chemistry is to fulfill societal needs without harming or depleting the planet's natural resources. However, there are other goals that should also be considered. In this instance, the emphasis is being moved to producing goods that can be completely recycled or reused. As one of the key objectives of green chemistry, initiatives are being done to reduce pollution and waste through altered production and consumption habits. Alternative technology development is essential to halting future harm to human health and the environment. In conclusion, the implementation of a green chemistry method can help to conserve the environment. However, putting the twelve principles of green chemistry into reality will finally assist to pave the road to a future where the grass is greener. Green chemistry alone cannot tackle the urgent environmental challenges and influences on our modern period.

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