University of Tikrit

Collage of science

Department of Chemistry

A scientific essay:-

Green Chemistry in Organic Synthesis

Papered by PhD student

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Green Chemistry

Green color is the color of chlorophyll and the color of the dollar. Being a green series of years is a battleground of environmental activists, and becoming a green becoming a trend in product marketing. And for chemists it becomes imperative to be green in applying the principles of green chemistry in all aspects of chemical sciences, in fundamental and applied research, production and education [(1)].

Definition of Green Chemistry

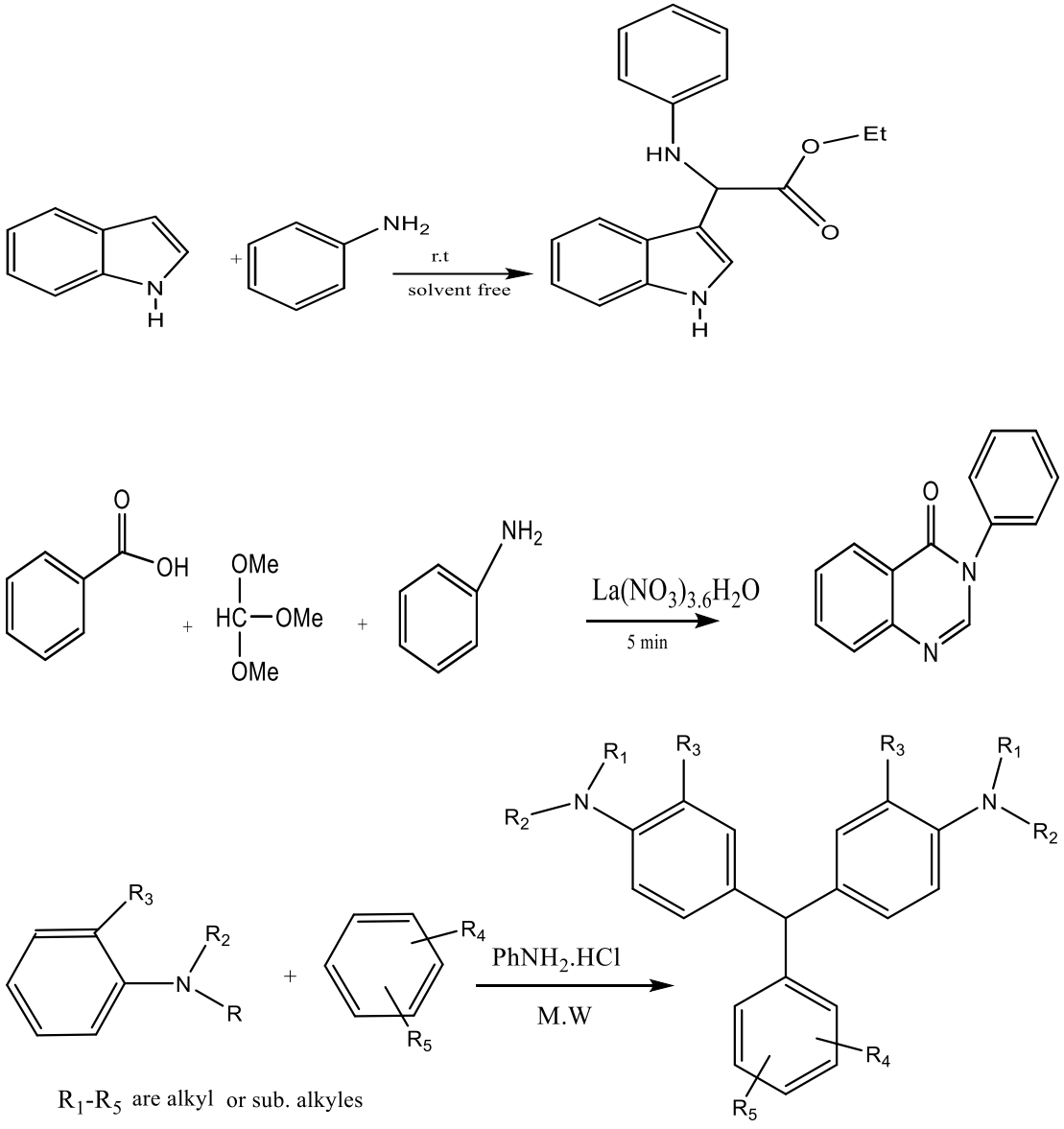
According to the EPA definition, green chemistry is defined as a chemistry that designs chemical products and processes that are harmless to the environment, thus preventing the formation of pollution. Chemical products should be made so that they do not remain in the environment at the end of their application and that they are broken down into components that are harmless to the environment. Saving based on efficient synthesis without the use of "exotic" reagents, reducing the required energy, and replacing organic solvents with water are significant even at the laboratory level, while in industrial scale possible millions of savings , Green chemistry is not a separate scientific discipline, but a responsible interdisciplinary approach to science, based on chemical, ecological and social responsibility, which enables creativity and the advancement of innovative research. [(1)]

Green and sustainable chemistry simply stated as “The design, synthesis and applications of chemical techniques and methodologies used for to minimize and reduced generation of feedstock, by-products, solvents, reagents that are harmful to human beings and environment”. To save our environment form the disadvantages of gray chemistry, green chemistry is the best alternative for green era of synthesis [(2)] .

THE CONCEPT OF GREEN CHEMISTRY

The Green Chemistry concept appeared in the USA as a general scientific program, originating from the interdisciplinary cooperation of research groups in universities, independent research groups, scientific societies

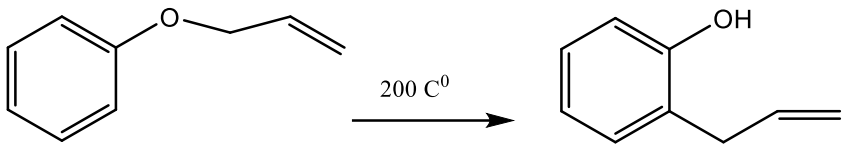
and government agencies, with members of each of these bodies having their own program dedicated to lowering
levels of environmental pollution. Green Chemistry comprises a new approach to the synthesis, processing and application of chemical substances, thus diminishing the hazards for human health and environmental pollution. veloped a synthesis of 4-quinazolinone **8** using a rapid method without solvent. “Grinding chemistry” has recently been reviewed [6]. An expanding area of chemistry without solvents involves the use of microwaves to irradiate mixtures of neat reagents. One example of this approach is the synthesis of 4,4'-diaminotriphenylmethanes **(3)**



Organic syntheses in the absence of solvent.

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. Chemists all over the world consider a reaction to be ‘perfect’ when the yield is 90% or more. However, such a reaction could create considerable amounts of waste. The concept of atom economy was developed by Trost and is represented as follows: % atom economy = (FW of the atoms used) (FW of the reactants in the reaction**)** [(3)]

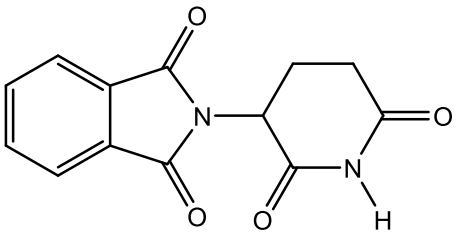


. Allylic rearrangement with 100% atom economy

Designing Safer Products

The design of products should be safe in terms of human health and the environment

A typical example of a hazardous drug is thalidomide which was introduced in 1961 in West Germany. This drug was prescribed to pregnant women against nausea and vomiting. Pregnant women who had taken the drug gave birth to babies with a condition called phocomelia – abnormally short limbs with toes sprouting from the hips and flipper-like arms. Other infants had eye and ear defects or malformed internal organs such as unsegmented small or large intestines .This drug is now prescribed for treatment of patients with multiple myeloma and for the acute treatment of the cutaneous manifestations of erythema nodosum leprosum [(3)]



Chemical structure of Thalidomide – 2-(2, 6-dioxopiperidin-3-yl)- 1,3-dion

History of Green Chemistry

In 1990 the Pollution Prevention Act was passed in the United States. This act helped create a modus operandi for dealing with pollution in an original and innovative way. This paved the way to the green chemistry concept. Paul Anastas and John Warner coined the two letter word "green chemistry" and developed the twelve principles of green chemistry. In 2005 Ryoji Noyori identified three key developments in green chemistry: use of supercritical carbon dioxide as green solvent, aqueous hydrogen peroxide for clean oxidations and the use of hydrogen in asymmetric synthesis (Anastas and Warner 1998). [4]

Concepts of Green Chemistry

The concept of green chemistry incorporates a new approach to the synthesis, processing and application of chemical substances in such manner as to reduce threats to health and environment. This new approach is also known as:

- Environmentally benign chemistry
- Clean chemistry
- Atom economy
- Benign-by-design chemistry

Green Chemistry or environmentally benign chemistry is the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances. Green chemistry was developed by virtue of the need to overcome this hazardous effect that toxic compounds exert on
the body. This relatively new area of chemistry uses water as the medium of chemical reactions that are done in the laboratory. Chemical reactions are usually done in a medium that is called solvent. An exception is reactions that take place in the gas phase where there is no need for medium there. Sometimes chemical reactions are done in a neat fashion. Namely, the reacting compounds are mixed and reacted together with the

need for a solvent. This is one of the methods that are used in green chemistry to avoid pollution and the hazardous effect of the volatile solvent. As a chemical philosophy, green chemistry applies to organic chemistry, inorganic chemistry, biochemistry, analytical chemistry and physical chemistry to minimize west, utilize renewable resources[5] .

Green Chemistry Principles:

1. Waste prevention instead of remediation
3. Use of less hazardous and toxic chemicals
4. Safer products by design
5. Innocuous solvents and auxiliaries
6. Energy efficiency by design
7. Preferred use of renewable raw materials
8. Shorter syntheses (avoid derivatization)
9. Catalytic rather than stoichiometric reagents
10. Design products to undergo degradation in the environment
11. Analytical methodologies for pollution prevention

In recent years, production and utilization of metabolites from microbial and plant origin have received increasing attention from different industrial sectors, such as fuel, pharmaceutical, food, and chemical [6]

China, too, has strict environmental concerns and has taken regulatory action on 40% of the industrial units located in thirty provinces
These changes in policy suggest that it has become imperative to follow green practices. [7]

Green chemistry in day-to-day life

Green Dry Cleaning of Clothes: Perchloroethylene (PERC) is commonly being used as a solvent for dry cleaning. It is now known that PERC which contaminates ground water and is a suspected carcinogen. A technology, known as Micell technology developed by Joseph De Simons, Timothy Romark, and James McClain made use of liquid CO2

and a surfactant for dry cleaning clothes, thereby replacing PERC. Dry cleaning machines have now been developed using this technique. Micell Technology has also evolved a metal cleaning system that uses CO2 and a surfactant thereby eliminating the need of halogenated solvents. [8]

Role of green chemistry in synthesis of drugs and chemicals to make ecofriendly

Microwave synthesis: Microwave assisted organic synthesis has revolutionized organic synthesis. Small molecules can be built in a fraction of the time required by classical thermal methods. As a result, this technique has rapidly gained acceptance as a valuable tool for accelerating drug discovery and development processes. A microwave is a form of electromagnetic energy, which falls at the lower end of the electromagnetic spectrum and is defined in a measurement of frequency as 300 to 300,000 Megahertz, corresponding to wavelengths of 1 cm to 1 m1. The microwave region of the electromagnetic spectrum lies between infrared and radio frequencies. Historically, chemists thought that compounds react only in the liquid state or if dissolved. This has made solvents common in chemical syntheses, however, many compounds used as solvents were found to be environmentally unfriendly. The problem associated with waste disposal of solvents has been overcome by performing reactions without a solvent under microwave irradiation (MWI). Coupling of MWI with the use of mineral-supported catalyzed reactions, under solvent-free conditions, provides clean chemical processes with the advantage of enhanced reaction rates, higher yields, greater selectivity, and greater ease of manipulation.[8]

Applications in Analytical Chemistry:

Microwave heating is extensively used for ashing in the petroleum and fuels, plastics, pharmaceuticals and food industries. In most of these industries, microwave powered muffle furnaces, which
are specifically meant for laboratory use, are used for ashing.[8]

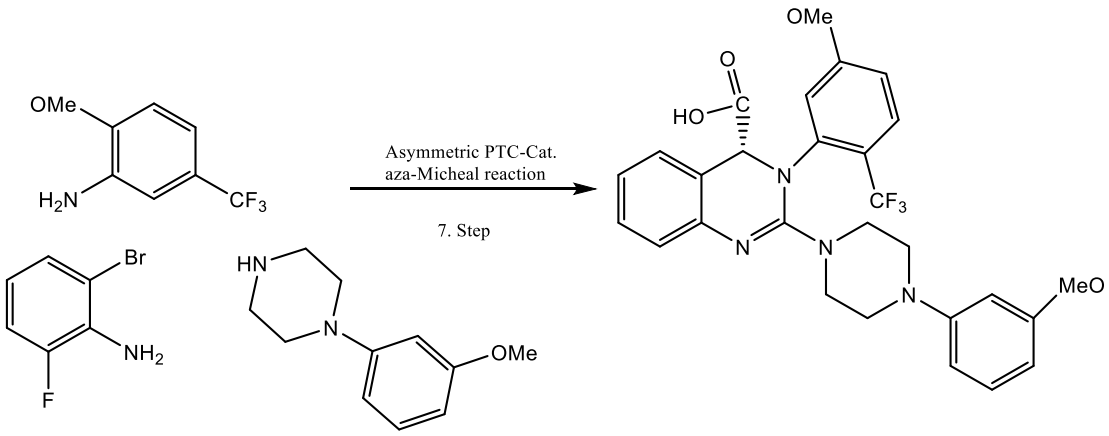
Drug	Approved in year	Biological actions
Captopril	1981	Antihypertensive
Dorzolamide	1995	Carbonic anhydrase inhibitors
Indinavir	1996	Human immunodeficiency virus (HIV)
Ritonavir	1996	Human immunodeficiency virus (HIV)
Saquinavir	1995	Human immunodeficiency virus (HIV)
Triofiban	1998	Fibronogen antagonist
Raltegravir	2007	Human immunodeficiency virus (HIV)
Zanamivir	1999	Neuramidase inhibitors
Aliskiren	2007	Human renin inhibitors
Boceprevir	PhaseIII Clinical trials	Hepatitis C VIRUS (HCV) Inhibitors
Nolatrexed	PhaseIII Clinical trials	Liver cancer
TMI-005	PhaseII Clinical trials	Rheumatoid arthritis
Oseltamivir	1999	Active against influenza A and B viruses
LY-517717	PhaseII Clinical trials	Serine protease inhibitor
NVP-AUY922	PhaseI Clinical trials	Inhibitor for HSP90

Table1: List of clinically approved drugs discovered by CADD

Industrial applications of green chemistry

The 20th century has seen a phenomenal growth of global economy and a continuous improvement of standard of living in the industrialized countries. The increasingly competitive
economic outlook and the shrinking graph of natural resources on the planet pose an urgent need to reduce the energy expenditure as well the production of waste. Sustainability is one of the main drivers for innovations in order to allow the technical industries to work for the well-being of consumers in a safe and healthy environment. The most attractive concept towards achieving sustainability is "Green Chemistry"—a term coined at United States Environmental Protection Agency by Anastas and Warner. [9]

Green Chemistry is not a lab-curiosity; instead it aims at big objective of creating a sustainable tomorrow. Increasing number of green methodologies developed by academic
and industrial researchers enables companies to commercialize these ideas. Industry, from small businesses to large corporations, has already made strategic moves towards sustainability by adopting the principles of green chemistry. The development of less hazardous processes and commercial products, the shift from inefficient chemical routes towards bio-based synthesis, and the replacement of oil-based feed stocks by renewable starting materials are only a few examples of the major decisions taken that will ultimately have vast consequences for the world chemical markets. As per the analysis of Environmental Protection Agency, the US drug industry has decreased the use of VOCs by 50% between 2004 and 2013 by adopting principles of green chemistry. In the same time span, the amount of chemical waste released to air, land and water decreased by 7% as per Toxics Release Inventory (TRI) of EPA



Green synthesis of Letermovir

a stereogenic center, the use of nine different solvents, high palladium loading in Heck coupling. Moreover, no recycling of solvents and reagents had been there in the scheme **(9)**

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