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"REVIEW ON GREEN CHEMISTRY APPROACH"

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ABSTRACT

Over the past few years, the chemistry community has been mobilized to develop new chemistry that is less hazardous to human health and the environment. This new approach has received extensive attention and goes by many names including Green Chemistry, Environmentally Benign Chemistry, Clean Chemistry, Atom Economy and Benign by Design Chemistry. Under all of these different designations there is a movement toward pursuing chemistry with the knowledge that the consequences of chemistry do not stop with the properties of the target molecule or the efficacy of a particular reagent. One obvious but important point- nothing is benign. All substances and all activity have some impact just by their being. What is being discussed when the term benign by design or environmentally benign chemistry is used is simply an ideal. Striving to make chemistry more benign wherever possible is merely a goal. Much like the goal of "zero defects" that was espoused by the manufacturing sector, benign chemistry is merely a statement of aiming for perfection. While it has already been mentioned that nothing is truly environmentally benign, there are substances that are known to be more toxic to humans and more harmful to the environment than others. By using the extensive data available on human health effects and ecological impacts for a wide variety of individual chemicals and chemical classes, chemists can make informed choices as to which chemicals would be more favourable to use in a particular synthesis or process. Simply stated, *Green Chemistry is the use of chemistry techniques and methodologies that reduce or eliminate the use or generation of feedstock, products, by-products, solvents, reagents, etc., that are hazardous to human health or the environment.* Green Chemistry is an approach to the synthesis, processing and use of chemicals that reduces risks to humans and the environment. Much innovative chemistry has been developed over the past several years that are effective, efficient and more environmentally benign. These approaches include new synthesis and processes as well as new tools for instructing aspiring chemists how to do chemistry in a more environmentally benign manner. The benefits to industry as well as the environment are all a part of the positive impact that Green Chemistry is having in the chemistry community and in society in general.

It is important that chemists develop new Green Chemistry options even on an incremental basis. While all elements of the lifecycle of a new chemical or process may not be environmentally benign, it is nonetheless important to improve those stages where improvements can be made. The next phase of an investigation can then focus on the elements of the lifecycle that are still in need of improvement. Even though a new Green Chemistry methodology does not solve at once every problem associated with the lifecycle of a particular chemical or process, the advances that it does make are nonetheless very important. Green Chemistry that possesses the spirit of sustainable development was booming in the 1990s, and has attracted more and more interest in the 21st century. The study of the organic reactions from the point of view of its greenness must have in mind first of all that a general synthetic method must be based on complete and efficient conversions of well defined selectivity and that greenness is more a term for comparison than an absolute kind of qualification. In order to evaluate the greenness of a particular process attention must be paid in the first instance to issues related to safety, health and protection of the environment, due to reactants (substrates and reagents), auxiliaries (mainly solvents) and waste. This enumeration is obviously incomplete, but can be useful at present. The question about how green a reaction is most frequently refers to a particular conversion, to the comparison between two or more alternative processes for the same synthetic target, or between the synthetic pathways for the manufacture of alternative compounds. The study of the greenness of the organic reaction is completed by a short overview of recent contributions intended to achieve efficient, safe and clean conversions that are susceptible to becoming general synthetic procedures.

With the increasing concerns about the environmental protection, synthesis of organic compounds from raw materials through a Green Chemistry procedure is desirable. Certainly the area of environmentally benign solvents has been one of the leading research areas of Green Chemistry with great advances seen in aqueous (biphase) catalysis and the use of supercritical fluids in chemical reactions. While the greenness of ionic liquids and fluorinated media will ultimately depend on their individual properties with respect to health and the environment, the sustainability of new biobased solvents has to be proven as well. There has been a renewed focus on the age-old pursuit of the organic chemist to design and successfully apply the ideal synthesis in terms of efficiency, with atom and step economy being a major goal. New catalytic processes continue to emerge to advance the goals of Green Chemistry, while techniques such as microwave and ultrasonic synthesis as well as in situ spectroscopic methods has been used extensively, leading to spectacular results. These research areas are a glimpse of some of the many topics directly relevant to Green Chemistry being pursued by researchers around the world. The development of asymmetric reactions stereoselective formation of C-C bond based on green protocol is also of paramount interest. In recent year's asymmetric metal, organo-metal catalysis has been intensively studied and several efficient methods for the synthesis of enantiomerically pure compounds have been developed. Our work which is based on green protocol by developing metal and organo-metal promoted synthesis of some organic compounds in aqueous media is also described. This chapter provides background to the present work by reviewing literature on Green Chemistry. The concept of Green Chemistry, its principles and different types of reactions are presented.

KEY WORDS: Fluorous phase, 1,4-Dihydropyridines, 3-Acetyl-4-hydroxycoumarin, 3-Acetyl-4-hydroxycoumarin, cetyltrimethylammonium chloride

Definition

The term Green Chemistry is defined as -“*The invention, design and application of chemical products and processes to reduce or to eliminate the use and generation of hazardous substances*”. While this short definition appears straightforward, it marks a significant departure from the manner in which environmental issues have been considered or ignored in the up-front design of the molecules and molecular transformations that are at the heart of the chemical enterprise. Looking at the definition of Green Chemistry, the first thing one sees is the concept of invention and design. By requiring that the impacts of chemical products and chemical processes are included as design criteria, the definition of Green Chemistry inextricably links hazard considerations to performance criteria. Another aspect of the definition of Green Chemistry is found in the phrase “use and generation”. Rather than focusing only on those undesirable substances that might be inadvertently produced in a process; Green Chemistry also includes all substances that are part of the process. Therefore, Green Chemistry is a tool not only for minimizing the negative impact of those procedures aimed at optimizing efficiency, although clearly both impact minimization and process optimization are legitimate and complementary objectives of the subject. Finally, the definition of Green Chemistry includes the term “hazardous”. It is important to note that Green Chemistry is a way of dealing with risk reduction and pollution prevention by addressing the intrinsic hazards of the substances rather than those circumstances and conditions of their use that might increase their risk. The definition of Green Chemistry also illustrates another important point about the use of the term “hazard”. This term is not restricted to physical hazards such as explosiveness, flammability, and corrosibility, but certainly also includes acute and chronic toxicity, carcinogenicity, and ecological toxicity. Furthermore, for the purposes of this definition, hazards must include global threats such as global warming, stratospheric ozone depletion, resource depletion and bioaccumulation, and persistent chemicals. To include this broad perspective is both philosophically and pragmatically consistent. It would certainly be unreasonable to address only some subset of hazards while ignoring or not addressing others. But more importantly, intrinsically hazardous properties constitute those issues that can be addressed through the proper design or redesign of chemistry and chemicals.

Green Chemistry definitions change based upon focus. Green Chemistry is often described within the context of new technologies. But Green Chemistry is not beholden to ionic liquids, microwave chemistry, supercritical fluids, bio-transformations, fluorinated phase chemistry, or any other new technology. Green Chemistry is outside of techniques used but rather resides within the intent and the result of technical application. Some view Green Chemistry as something process chemists do already.... Good process chemistry. While often enabling “greener” synthesis, good process chemistry is not equivalent to Green Chemistry. A robust, efficiency, and cost-effective chemical process is likely accepted as good process chemistry. Green Chemistry is not simply good process chemistry; it is the highest efficiency potential that exists for each chemical process, serving as both an inspiration for and a measure of the best process chemistry. Others feel Green Chemistry is a purely environmental agenda, and a condemnation of industrial chemistry or of scientists. This picture neglects the direct relationship between Green Chemistry principles and highly efficient and environmentally benign chemistry.

Green Chemistry is defined as environmentally benign chemical synthesis. Green Chemistry may also be defined as the invention, design, and application of chemical products and processes to reduce or eliminate the use and generation of hazardous substances. The synthetic schemes are designed in such a way that there is least pollution to the environment. As on today, maximum pollution to the environment is caused by numerous chemical industries. The cost involved in disposal of the waste products is also enormous. Therefore, attempts have been made to design synthesis for manufacturing processes in such a way that the waste products are minima, they have no effect on the environment and their disposal is convenient. For carrying out reactions it is necessary that the starting materials, solvents and catalysts should be carefully chosen. For example, use of benzene as a solvent must be avoided at any cost since it is carcinogenic in nature. If possible, it is best to carry out reactions in the aqueous phase. With this view in mind, synthetic methods should be designed in such a way that the starting materials are consumed to the maximum extent in the final product. The reaction should not generate any toxic by-products. Since its birth over a decade ago, the field of Green Chemistry has seen rapid expansion, with numerous innovative scientific breakthroughs associated with the production and utilization of chemical products. The concept and ideal of Green Chemistry now goes beyond chemistry and touches subjects ranging from energy to societal sustainability. The key notion of Green Chemistry is “efficiency”, including material efficiency, energy efficiency, manpower efficiency, and property efficiency (e.g., desired function vs toxicity). Any “wastes” aside from these efficiencies are to be addressed through innovative Green Chemistry means. “Atom-economy” and minimization of auxiliary chemicals, such as protecting groups and solvents, form the pillar of material efficiency in chemical productions. Green Chemistry is an approach to the design, manufacture and use of chemical products to intentionally reduce or eliminate chemical hazards. Goal of Green Chemistry is to create better, safer chemicals while choosing the safest, most efficient ways to synthesize them and to reduce wastes. Chemicals are typically created with the expectation that any chemical hazards can somehow be controlled or managed by establishing “safe” concentrations and exposure limits.

PRINCIPLES OF GREEN CHEMISTRY

Green Chemistry aims to eliminate hazards right at the design stage. The practice of eliminating hazards from the beginning of the chemical design process has benefits for our health and the environment, throughout the design, production, use/reuse and disposal processes.²⁹ Practitioners of Green Chemistry strive to protect the environment by cleaning up toxic waste sites and by inventing new chemical methods that do not pollute and that minimize the consumption of energy and natural resources. In 1998, two US chemists, Dr. Paul Anastas and Dr. John Warner outlined Twelve Principles of Green Chemistry to demonstrate how chemical production could respect human health and the environment while also being efficient and profitable. Guidelines for developing Green Chemistry technologies are summarized in the “Twelve Principles of Green Chemistry,” shown in the following.

1. It is better to prevent waste than to treat or clean up waste after it is formed. It is most appropriate to carry out a synthesis by following a pathway so that formation of waste is minimum or absent. One type of waste product common and often avoidable is the starting material or reagent that remains unreacted. The well-known saying “Prevention is better than cure should be followed”.

2. Synthetic methods should be designed to maximize the incorporation of all the materials used in the process into the final product. If one mole of the starting material produces one mole of the product, the yield is 100 %. However, such a synthesis may generate significant amount of waste or by product which is not visible in the above calculation. Such a synthesis, even though gives 100% yield, is not considered to be green synthesis. In order to find, if a particular reaction is green, the concept of atom economy was developed by Barry Trost of Stanford University. This considers the amount of starting materials incorporated into the desired final product. Thus by incorporation of greater amounts of the atoms contained in the starting materials (reactants) in to the formed products, fewer waste by products are obtained. In this way, using the concept of atom economy along with ideas of selectivity and yield, “greener” more efficient synthesis can be developed. The atom economy for a reaction can be calculated using the following equation:

$$\text{Percent atom economy} = \frac{\text{Molecular weight of desired product}}{\text{Molecular weights of all reactants}} \times 100\%$$

To illustrate the benefits of atom economy, consider the synthesis of ibuprofen. In the former process, developed in the 1960s, only 40% of the reactant atoms were incorporated into the desired ibuprofen product; the remaining 60% of the reactant atoms found their way into unwanted by-products or waste that required disposal. The new method requires fewer reaction steps and recovers 77% of the reactant atoms in the

desired product. This 'green' process eliminates millions of pounds of waste chemical by-products every year, and it reduces by millions of pounds the amount of reactants needed to prepare this widely used analgesic.

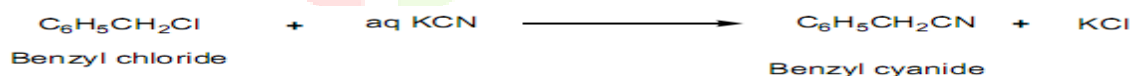
3. Whenever practicable synthetic methodologies should be designed to use and generate a substance that poses little or no toxicity to human health and the environment. Wherever practicable, synthetic methodologies should be designed to use and generate substances that pose little or no toxicity to human health and the environment. Redesigning existing transformations to incorporate less hazardous materials is at the heart of Green Chemistry.

4. Chemical products should be designed to preserve efficiency of function while reducing toxicity. The designing of safer chemical is now possible since there have been great advances in the understanding of chemical toxicity. It is now fairly understood that a correlation exist between chemical structure e.g. presence of functional groups and the existence of toxic effects. The idea is to avoid the functionality related to the toxic effect. Chemical properties of a molecule, such as water solubility, polarity etc. so that they can manipulate molecules to the desired effects.

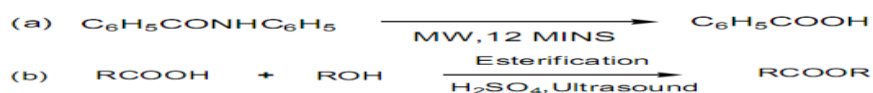
5. The use auxiliary substances (e.g. solvents, separating agents) should be made unnecessary wherever possible and innocuous when used. An auxiliary substance is one that helps in manufacture of a substance, but does not become an integral part of the chemical. Such substances are used in the manufacture, processing at every step. Major problem with many solvents is their volatility that may damage human health and the environment. Even processes like recrystallisation require energy and substances to change the solubility. The problem of solvents has been overcome by using such solvents which do not pollute the environment. Such solvents are known as green solvents. Examples include liquid carbon dioxide (supercritical CO₂), ionic liquid water. Even reactions have been conducted in solid state. For example the condensation reaction of ortho-esters with o-phenylenediamines in presence of KSF clay under solvent free conditions using microwave.

Many solvents used in traditional organic synthesis are highly toxic. The Green Chemistry approach to the selection of solvents has resulted in several strategies. One method that has been developed is to use supercritical carbon dioxide as a solvent. Supercritical carbon dioxide is formed under conditions of high pressure in which the gas and the liquid phases of carbon dioxide combine to a single –phase compressible fluid that becomes an environmentally benign solvent (temperature 31°C, 7280 kPa, or 72 atmospheres). Supercritical CO₂ has remarkable properties. It behaves as a material whose properties are intermediate between those of a solid and those of a liquid. The properties can be controlled by manipulating temperature and pressure. Supercritical CO₂ is environmentally benign because of its low toxicity and easy recyclability. Carbon dioxide is not added to the atmosphere; rather, it is removed from the atmosphere for use in chemical processes. It is used as a medium to carry out a large number of reactions that would otherwise have many negative environmental consequences. It is even possible to perform stereoselective synthesis in supercritical CO₂. Some reactions can be carried out in ordinary water, the most green solvent possible. Recently, there has been much success in using near-critical water at higher temperatures where water behaves more like an organic solvent. Eckert and Liotta were able to run Friedel-Crafts reactions in near –critical water without the need for the acid catalyst AlCl₃, which is normally used in large amounts in these reactions. In the past 5 years, many new ionic liquids have been developed with a broad range of properties. By selecting the appropriate ionic liquid, it is now possible to carry out many types of organic reactions in these solvents. In some reactions, a well –designed ionic solvent can lead to better yields under milder conditions than is possible with traditional solvents. Another approach to making organic chemistry greener involves the way in which a reaction is carried out, rather than in the selection of starting material, reagents, or solvents. Microwave technology can be used in some reactions to provide the heat energy required to make the transformation go to completion. With microwave technology, reactions can take place with less toxic reagents and in a shorter time, with fewer side reactions, all goals of Green Chemistry. Microwave technology has also been used to create supercritical water that behaves more like an organic solvent and could replace more toxic solvents in carrying out organic reactions. Another Green Chemistry approach is the use of a catalyst which facilitates transformations without the catalyst being consumed in the reaction and without being incorporated in the final product. Therefore, use of catalyst should be preferred whenever possible.

6. Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Energy generation, as we know has a major environmental effect. The requirement of energy can be kept to a base minimum in certain cases by the use of a catalyst. For example in conversion of benzyl chloride into benzyl cyanide if we use phase transfer catalyst, the conversion goes to completion in a very short time.



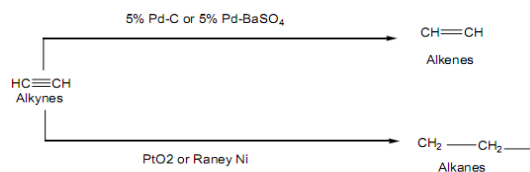
Conventionally, we have been carrying reaction by heating on wire gauze, in oil bath or heating mantels. It is now possible that the energy to a reaction can be supplied by using microwaves, by sonication or photo chemically. Simple examples are,



7. A raw material or feedstock should be renewable rather than depleting, whenever technically and economically practicable. Non reversible or depleting sources can exhausted by their continual use. So these are not regarded as sustainable from environmental point of view. The starting materials which are obtained agricultural or biological processes are referred to as renewable starting materials. Substances like carbon dioxide (generated from natural sources or synthetic routes like fermentation etc) and methane gas (obtained from natural sources such as marsh gas, natural gas etc) are available in reasonable amounts and so are considered as renewable starting material. Methane, a constituent of biogas and natural gas can easily be converted into acetylene by partial combustion. Acetylene is a potential source of number of chemicals such as ethyl alcohol, acetaldehyde, vinyl acetate etc.

8. Unnecessary derivatization (blocking group, protection, deportation, temporary modification of physical/chemical processes) should be avoided whenever possible. A commonly used technique in organic synthesis is the use of protecting or blocking group. These groups are used to protect a sensitive moiety from the conditions of the reaction, which may make the reaction to go in an unwanted way if it is left unprotected. This procedure adds to the problem of waste disposal.

9. Catalytic reagents (as selective as possible are superior to stoichiometric reagents. The catalyst as we know facilitates transformation without being consumed or without being incorporated into the final product. Catalysts are selective in their action in that the degree of reaction that takes place is controlled, e.g. mono addition v/s multiple addition. A typical example is that reduction of triple bond to a double bond or single bond.

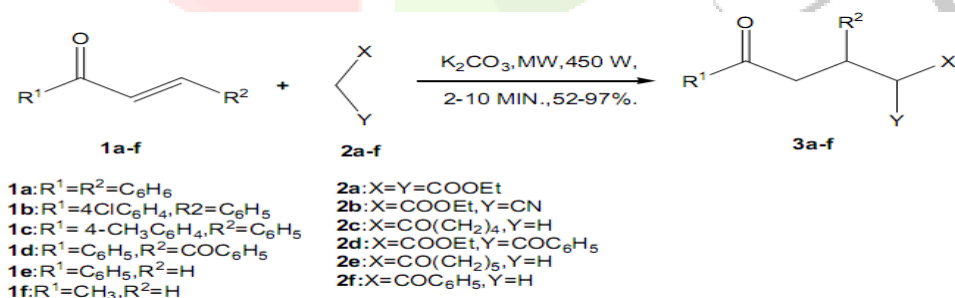


In addition to the benefits of yield and atom economy, the catalysts are helpful in reducing consumption of energy. Catalysts carry out thousands of transformation before being exhausted.

10. Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products. It is extremely important that the products designed to be synthesized should be biodegradable. They should not be persistent chemicals or persistent bio accumulators. It is now possible to place functional groups in a molecule that will facilitate its biodegradation. Functional groups which are susceptible to hydrolysis, photolysis or other cleavage have been used to ensure that products will be biodegradable. It is also important that degradation products do not possess any toxicity and detrimental effects to the environment. Plastic, Pesticides (organic halogen based) are examples which pose to environment.

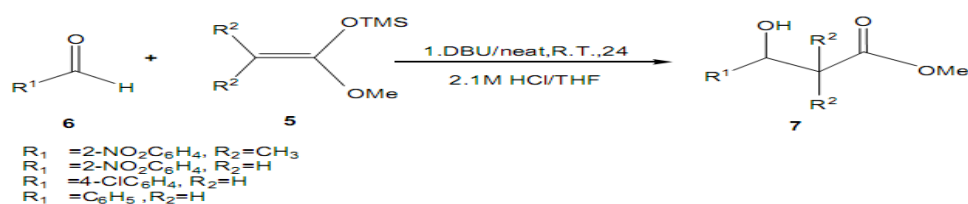
SOLVENT FREE REACTIONS

Environmental concerns in synthetic chemistry have led to a reconsideration of reaction methodologies. This has resulted in investigations into atom economy, the use of supercritical CO_2 , ionic liquids and other procedures to reduce the disposal problems associated with most chemical reactions. One obvious route to reduce waste entails generation of chemicals from reagents in the absence of solvents. Therefore the design of green processes with no use of hazardous and expensive solvents, e.g., "solvent-free" reactions, has gained special attention from synthetic organic chemists. As a result, many reactions are newly found to proceed cleanly and efficiently in the solid state or under solvent-free conditions. Less chemical pollution, lower expenses, and easier procedures are the main reasons for the recent increase in the popularity of solvent-free reactions. While an obvious approach to chemical synthesis, there are many problems associated with this approach, the chief of which is the role of diffusion/interactions between reactants. Further, it is never clear that the reactions in the solid state will generate the same products as those found in the presence of solvents. Generally, Michael additions are conducted in a suitable solvent in the presence of a strong base either at room temperature or at elevated temperatures. Due to the presence of the strong base, side reactions such as multiple condensations, polymerizations, rearrangements and retro-Michael additions are common. These undesirable side reactions decreases the yields of the target adduct and render their purification difficult. Better results can be obtained by employing weaker bases such as piperidine, quaternary ammonium hydroxide, tertiary amines etc. There have been some reports on Michael reactions catalyzed by potassium carbonate in organic solvents, 40 and water in the presence of surfactants or phase-transfer catalysts. To a large extent, mild bases restrain the formation of side products, thus improving the yield of the desired Michael adducts. Recently, non-conventional procedures like conducting the reaction on the surface of a dry medium or under microwave irradiation were found to facilitate the Michael reaction. For the purposes of eco-friendly "Green Chemistry", a reaction should ideally, be conducted under solvent-free conditions with minimal or no side-product formation and with utmost atom-economy. Even though microwave assisted solvent-free Michael addition reactions on BiCl_3 or CdI_2 , EuCl_3 , $\text{CeCl}_3 \cdot 5\text{H}_2\text{O}$ and alumina surfaces are known. Rao and Jothilingam have studied Michael addition of some active methylene compounds (2a-f) to four Michael acceptors (1a-f) viz (i) 1, 3-diphenyl-2-propene-1-one (chalcone), (ii) phenyl vinyl ketone, (iii) 1, 4-diphenyl-2-butene-1,4-dione (dibenzoyl ethylene), and (iv) methyl vinyl ketone on potassium carbonate surface under microwave irradiation (Scheme 1).



Scheme 1

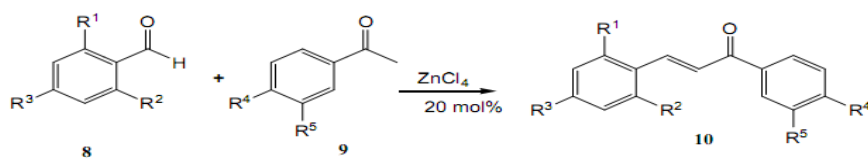
Loh et al. have developed an efficient and environmentally friendly protocol for Mukaiyama aldol reaction of ketene silyl acetyls (5) with different aldehydes (6) in the presence of a catalytic amount of DBU under solvent free conditions at room temperature (Scheme 2).



Scheme 2

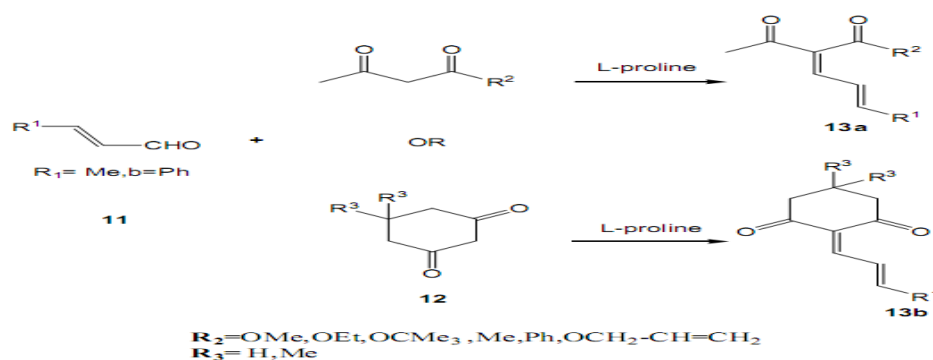
Atul Kumar and Akanksha described Zirconium chloride to be a new and highly efficient catalyst which catalyzed aldol reaction of appropriately substituted aromatic aldehydes (8) with a broad variety of aromatic ketones (9) to obtain the corresponding 1, 3-diaryl-2-propenones (10) with good to excellent yields in short span of time without the formation of any side product under solvent free conditions, at

room temperature. The reaction is very fast, clean and environmentally benign for the synthesis of variety of 1,3-diaryl-2-propenones. Zirconium chloride also found to be compatible with various solvents and gave the aldol product in acceptable yield (56–70%) but the excellent yield was obtained in solvent free condition. The higher mol% of the catalyst (zirconium chloride) yielded the 1, 4-Michael adduct along with the aldol product (Scheme 3).



Scheme 3

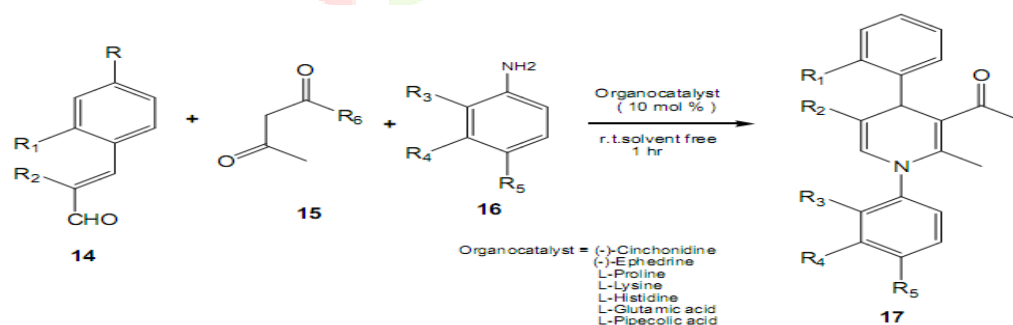
Goswami and Das reported a series of conjugated dienones and enones which were synthesized by a reaction of both conjugated and simple aldehydes, respectively, with 1,3-dicarbonyl compounds (11) and aldehydes (12) under solvent-free conditions at room temperature in the presence of 10 mol % of L-proline as catalyst. All the products were obtained selectively as E-isomers with the exception of allyl acetoacetate which gave a mixture of both E and Z isomers with an E-isomer in the predominant form (Scheme 4).



Scheme 4

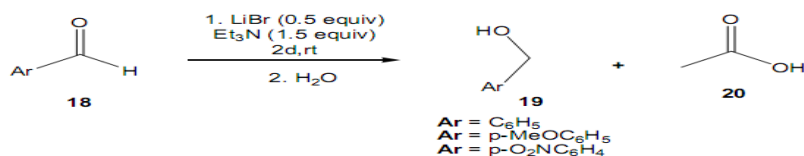
The multi-component reactions (MCRs) involve three or more reactants which are combined together in a single reaction flask to generate a product incorporating most of the atoms contained in the starting material. Due to intrinsic atom economy, selectivity underlying such reaction, simpler procedure, equipment, time and energy saving as well as environmental friendliness MCRs are gaining much importance in both academia and industry. 1, 4-Dihydropyridines (1, 4-DHPs) and their derivatives are important class of bioactive molecules in the field of drug and pharmaceuticals. These compounds are well known as calcium channel modulators and have emerged as one of the most important classes of drugs for the treatment of hypertension. 1,4-Dihydropyridine derivatives possess a variety of biological activities such as HIV protease inhibition, MDR reversal, adipoprotection, vasodilator, antitumour, bronchodilator and hepatoprotective activity.

The catalytic property of small organic molecules like cinchona alkaloids and amino acids have been shown as quite promising and highly efficient organocatalysts for multi-component reactions. Recently, Atul Kumar⁷¹ and Ram Awatar Maurya reported an organocatalysed multi-component reaction of an aldehyde (14), acetoacetate ester (15), cyclic 1,3-diketone (16) and ammonium acetate to form polyhydroquinoline derivatives (17). Thus, they use the organocatalysts for the multi-component reaction of acetoacetate ester, cinnamaldehyde and anilines to yield N-aryl 5-unsubstituted or 5,6-unsubstituted 1,4-dihydropyridines (Scheme 5). The reaction is generally very fast and the products are obtained in high yield. The catalytic activity of small organic molecules like amino acids (acidic, basic and neutral), ephedrine and cinchona alkaloids was studied.



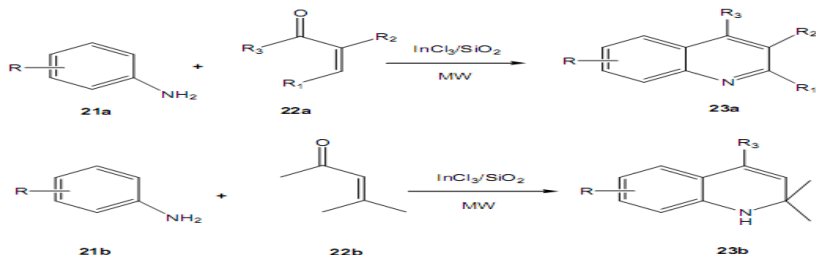
Scheme 5

Recent developments in the classical Cannizzaro reaction involve the use of various Lewis acidic reagents, heterogeneous catalytic systems, and supercritical solvents. Mojtahedi et al. reported that a selective conversion of aldehydes (18) with no α -hydrogen to their respective alcohols (19) and/or carboxylic functionalities (20) of choice is practically attainable under catalysis of lithium bromide (LiBr) in the presence of triethylamine (Et₃N) at room temperature in a solvent free environment (Scheme 6).



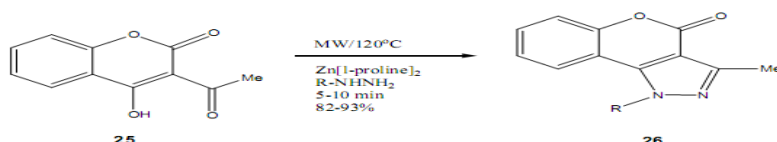
Scheme 6

Ranu et al. reported a convenient and efficient procedure for the synthesis of quinolines and dihydroquinolines (23a, 23b) by a simple one-pot reaction of anilines (21a, 21b) with alkyl vinyl ketones (22a, 22b) on the surface of silica gel impregnated with indium(III) chloride under microwave irradiation without any solvent (Scheme 7).



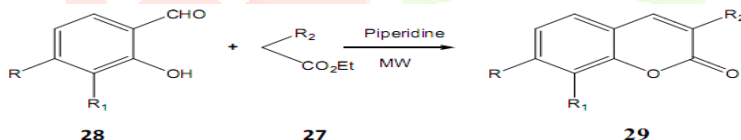
Scheme 7

Manvar et al. described the hydrazones of 3-acetyl-4-hydroxycoumarin (24) undergo ring cyclization to give 3-methyl-1-substituted phenyl-1H-chromeno [4,3- c]pyrazol-4-ones (25) under the influence of microwave irradiation by using Zn [lproline]2, a novel Lewis acid catalyst. The overall yields of the products were found to be 82–93%. Without use of the catalyst, no reaction progress was observed. The reusability of the catalyst was also checked and found up to seven cycles (Scheme 8).



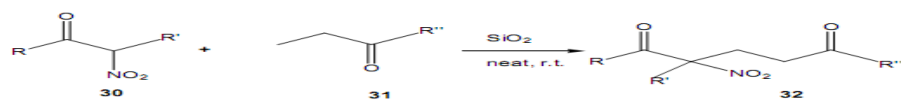
Scheme 8

Villemin and Martin have synthesized 5-nitrofurfurylidine by the condensation of 5-nitrofurfuraldehyde with active methylene compounds under microwave irradiation using K₁₀ and ZnCl₂ as a catalyst. The useful synthesis coumarins via the microwave promoted Pechmann reaction 84a has been extended to solventless systems wherein salicylaldehydes (28) undergo Knoevenagel condensation with a variety of ethylacetate derivatives (27) under basic conditions (piperidine) to afford coumarins (29) (Scheme 9).



Scheme 9

Ballini et al. reported the Conjugate addition of both linear and cyclic α -nitro ketones (30) to conjugated enones (31) under heterogenous, solvent-free and mild acidic conditions by mixing at room temperature stoichiometric amounts of substrates with silica (silica/substrate = 350 mg mmol⁻¹) and leaving the mixture at room temperature for the suitable reaction time giving good yields of 2-nitro-1,5- diones (32) and it is worthy to note that no products arising from the cleavage of a nitro-cycloalkanones were observed under these reaction conditions (Scheme 10).



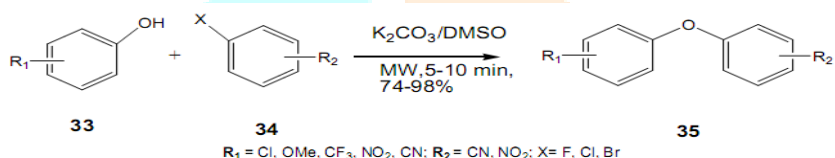
Scheme 10

MICROWAVE INDUCED GREEN SYNTHESIS

With increasing community concern over possible influences of chemicals and chemical practices on the environment microwave induced green synthesis has received considerable attention for direct, efficient, and environmentally unobtrusive synthesis. The first microwave-assisted organic syntheses was reported in 1986. By using this technique, considerably shorter reaction times than normal had been obtained for common organic transformations such as esterification, hydrolysis, etherification, addition, and rearrangement. Inadequate controls in the rudimentary equipment employed, however, generated hazards, including explosions. In the electromagnetic radiation spectrum, microwaves (0.3 GHz–300 GHz) lie between radio wave (Rf) and infrared (IR) frequencies with relatively large wavelength. Microwaves, a non-ionizing radiation incapable of breaking bonds, are a form of energy and not heat and are manifested as heat through their interaction with the medium or materials wherein they can be reflected (metals), transmitted (good insulators that will not heat) or absorbed (decreasing the available microwave energy and rapidly heating the sample). Microwave reactions involve selective absorption of electromagnetic waves by polar molecules, non-polar molecules being inert to microwaves. When molecules with a permanent dipole are submitted to an electric field, they become aligned and as the field oscillates their orientation changes, this rapid reorientation produces intense internal heating. The main difference between classical heating and microwave heating lies in core and homogenous heating associated with microwaves, whereas classical heating is all about heat transfer by preheated molecules. In microwave induced organic reactions, the reactions can be carried out in a

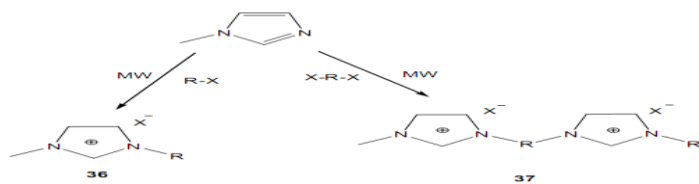
solvent medium or on a solid support in which no solvent is used. For reactions in a solvent medium, the choice of the solvent is very important.^{88,89} Microwave chemistry generally relies on the ability of the reaction mixture to efficiently absorb microwave energy, taking advantage of "microwave dielectric heating" phenomena such as dipolar polarization or ionic conduction mechanisms.⁹⁰ In most cases this means that the solvent used for a particular transformation must be microwave absorbing. The ability of a specific solvent to convert microwave energy into heat at a given frequency and temperature is determined by the so-called loss tangent ($\tan \delta$), expressed as the quotient, $\tan \delta = \epsilon''/\epsilon'$, where ϵ'' is the dielectric loss, indicative of the efficiency with which electromagnetic radiation is converted into heat, and ϵ' is the dielectric constant, describing the ability of molecules to be polarized by the electric field. A reaction medium with a high $\tan \delta$ at the standard operating frequency of a microwave synthesis reactor (2.45 GHz) is required for good absorption and, consequently, efficient heating.

Microwave ovens offer a clean and sometimes cheaper alternative to oil baths for many organic reactions. Microwave synthesis can be performed either under sealed-vessel or open-vessel conditions. Reactions performed in sealed vessels can reach temperatures much higher than the boiling point of the solvent used at elevated pressure. In open-vessel microwave assisted reactions, reactions are carried out at atmospheric pressure; yet solvents can still reach temperatures that are 10-20°C above their boiling points, which may be explained by the occurrence of instantaneous hot spots. An excellent solvent in a domestic microwave oven is N,N-dimethyl formamide (DMF) (b.p.160°C). Open-vessel synthesis allows for any gases that may be generated in a reaction to evolve from the reaction environment possibly causing reactions to progress further to completion than when performed in a sealed vessel. Also, open-vessel reactions can be performed using standard laboratory glassware, such as round-bottom flasks and reflux condensers, in the microwave cavity allowing reactions to be carried out on a larger scale. Since microwave synthesis was introduced in the literature, there has been an explosion of applications to organic synthesis, inorganic synthesis, and organometallic synthesis. Lopy has described a solvent free/microwave method for the synthesis of aromatic ethers by the S_NAr reaction of 4-nitro-substituted halogenobenzenes or 2-halophenylbenzenes, but only phenol was employed. Similar results have been achieved by Bogdal, who prepared a range of aromatic ethers by reaction of phenols with primary alkyl halides under microwave heating, however, in the presence of TBAB. Also Fan has employed the same strategy for the reaction of 1-chloro-4-nitrobenzene and phenolates, affording 4-nitrodiphenyl ethers. Li et al. reported the microwave-assisted coupling of phenols (33), including those having a strong electron-withdrawing group, with aryl halides (34) in the presence of potassium carbonate providing diverse diaryl ethers (35) with high to excellent yields within 5-10 min. (Scheme 11). Rather, the reaction under microwave irradiation is very clean and no by-products have been detected. Therefore, the workup procedure involves only a simple filtration of the precipitation followed by washing with water. In all instances, the products can be obtained in purity higher than 98% as indicated by GCMS and ¹H NMR analysis.



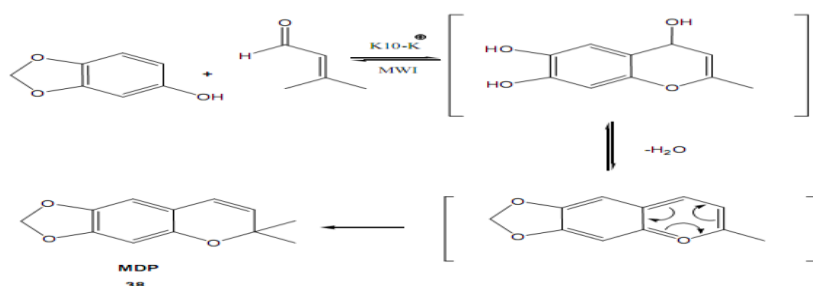
Scheme 11

The development of cleaner technologies is a major emphasis in Green Chemistry. The search for a non-volatile and recyclable alternative is thus holding a key role in this field of research. The use of fused organic salts, consisting of ions, is now emerging as a possible alternative. A proper choice of cations and anions is required to achieve ionic salts that are liquids at room temperature and are appropriately termed room-temperature ionic liquids (RTILs). Common RTILs consist of N,N'-dialkylimidazolium, alkylammonium, alkylphosphonium or N-alkylimidazolium as cations. Most of these ionic salts are good solvents for a wide range of organic and inorganic materials and are stable enough to air, moisture, and heat. Rajendra et al. reported an efficient method for the preparation of ionic liquids by simply exposing neat reactants in open glass containers to microwaves using an unmodified household MW oven. A general schematic representation for the preparation of mono (36) and dicationic (37) 1,3-dialkylimidazolium halides is depicted below (Scheme 12).



Scheme 12

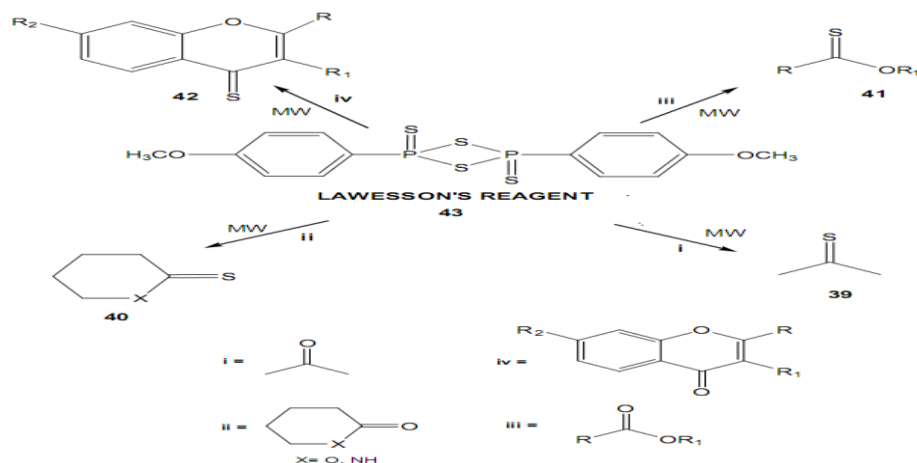
Matthew et al. reported a microwave-assisted, one-pot, solvent-free synthesis of methylenedioxyprococene (MDP) (38), a natural insecticide with antijvenile hormone activity in some insects, on basic Montmorillonite K10. It is a cleaner chemical reaction and forms an important component of Green Chemistry. The reported synthesis, a clay-catalyzed, microwave-assisted condensation of sea amol with 3-methyl-2-butenal (Scheme 13), is a unique example of Green Chemistry reaction.



Scheme 13

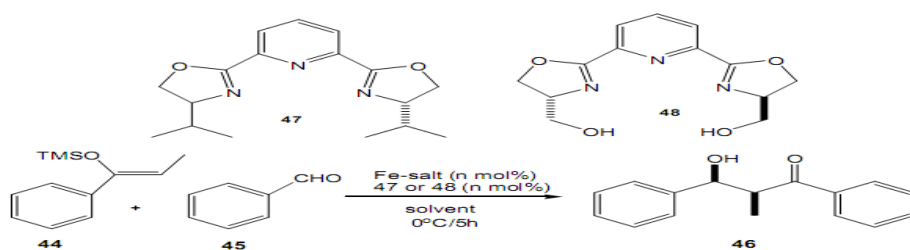
The application of microwave irradiation in conjunction with the use of catalysts or mineral-supported reagents, under solvent-free conditions, enables organic reactions to occur expeditiously at ambient pressure thus providing unique chemical processes with special attributes such as enhanced reaction rates, higher yields, and the associated ease of manipulation. Rajender S. Varma described the synthesis of thioketones (39),

thiolactones (40), thioamides, thionoesters (41), and thioflavonoids (42) simply by mixing the carbonyl compounds (i-iv) with neat Lawesson's reagent (0.5 equiv.) (43) and irradiating under solvent-free conditions that do not require any acidic or basic media giving high-yield conversion of ketones, flavones, isoflavones, lactones, amides, and esters to the corresponding thio analogs (Scheme 14).

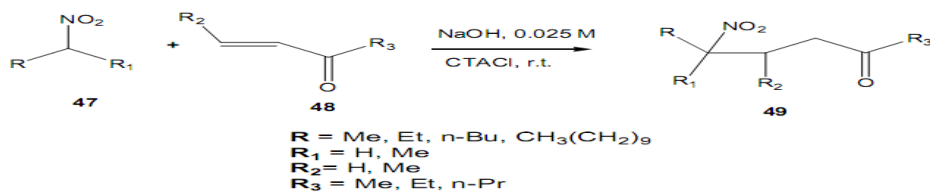


AQUEOUS MEDIATED SYNTHESIS

Aqueous mediated reactions offer useful and more environmentally friendly alternatives to their harmful organic solvent versions and have received increasing interest in recent years. Furthermore, water has unique physical and chemical properties, and by its utilization it would be possible to realize reactivity or selectivity that cannot be attained in organic solvents. Water is the most abundant, cheapest, and non-toxic chemical in nature. It has high dielectric constant and cohesive energy density compared to organic solvents. It has also special effects on reactions arising from inter and intramolecular non-covalent interactions leading to novel solvation and assembly processes. Water as a reaction medium has been utilized for large numbers of organic reactions. Utility of aqueous reactions is now generally recognized. It is desirable to perform the reactions of compounds containing water of crystallization or other water-soluble compounds in aqueous media, because tedious procedures to remove water are necessary when the reactions are carried out in organic solvents. Moreover, aqueous reactions of organic compounds avoid the use of harmful organic solvents. Thus; development of an efficient and convenient synthetic methodology in aqueous medium is an important area of research. Recent literature survey revealed that water as reaction solvent exhibit several applications on organic reactions such as Barbierallylation reaction mediated by several metals such as zinc, indium, manganese and others in aqueous medium, metal mediated reactions mediated by zinc, tin and indium in aqueous medium as reported by Wu et al. for the synthesis of metallic indium in situ via $\text{Sn/InCl}_3 \cdot 4\text{H}_2\text{O}$ system in THF- H_2O (8/1) mixture in open air and its application in reductive cyclodimerization of arylidenecyanoacetates to afford cyclopentamine derivatives with high stereo selectivity under milder conditions, in the synthesis of a great variety of thioether compounds with heterocycle having broad –spectrum biological activities such as fungicidal, insecticidal, herbicidal and plant growth regulative activities using metal catalyst in water, organocatalytic asymmetric direct aldol and Michael reaction in water by using L-proline based organocatalyst such as zinc-proline complex, dipeptide etc. Here a brief literature survey on various organic reactions in aqueous media is highlighted. Since Kobayashi showed that a chiral copper complex can act as a water tolerant catalyst for the Mukaiyama–aldol reaction, several other Lewis acids have been utilized in asymmetric aldol reactions in aqueous solvents. More recently, Kobayashi reported that Fe(II) and Fe(III) salts showed considerable activity in stereoselective Mukaiyama–aldol reactions in aqueous THF, especially when the reaction was carried out in the presence of catalytic amounts of surfactants. Jankowska et al. reported recently the application of a zinc-based chiral Lewis acid in an asymmetric Mukaiyama–aldol reaction in aqueous media. They described a water stable chiral Lewis acid (47) containing an iron (II) ion and a pybox-type ligand. The resulting cationic aqua complex of C2-symmetry is an effective Lewis acid catalyst for asymmetric Mukaiyama–aldol reactions in aqueous media. The aldol products (46) have been obtained in good yields, syn-diastereoselectivities and ca. 70% levels of enantioselectivity by reacting silylenol ether (44) with benzaldehyde (45) (Scheme 15).

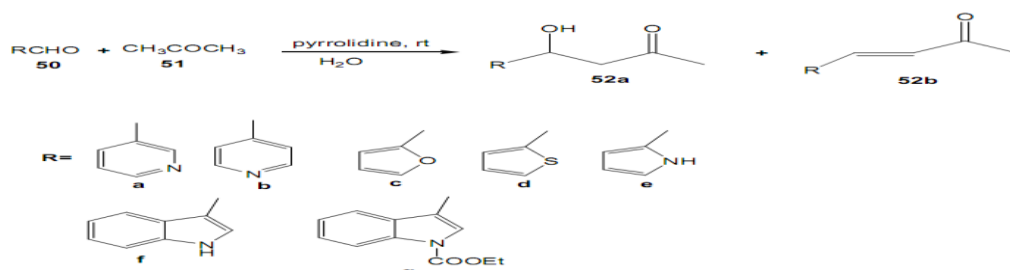


In recent years, there has been increasing recognition that water is an attractive medium for many organic reactions. The aqueous medium with respect to organic solvents is less expensive, less dangerous and environment friendly, while it allows a right control of the pH. In addition, the low solubility of most reagents in water is not an obstacle to the reactivity which, on the contrary, is often improved. Recently, Lubineau and Auge published the first example of the Michael addition of nitroalkanes in water with the help of sugars. Roberto et al. described that the Michael reaction of various nitroalkanes (47) with conjugated enones (48) can be performed in aqueous media using a solution of sodium hydroxide 0.025 M in the presence of catalytic amount of cetyltrimethylammonium chloride (CTACl) as cationic surfactant giving products (49) with good yield (Scheme 16).

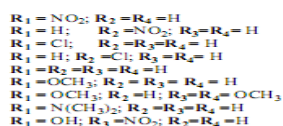
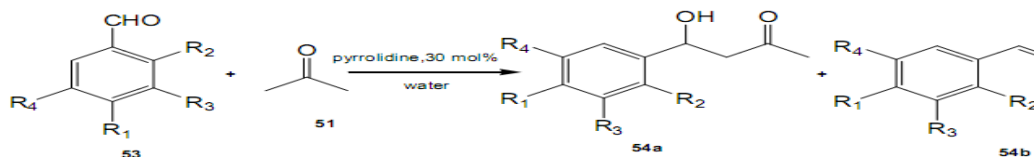


Scheme 16

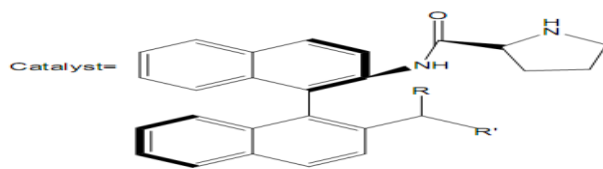
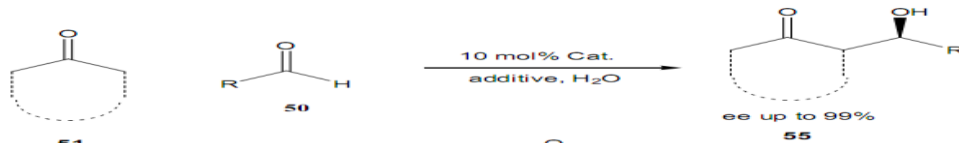
Recently, Janda and Barbas have reported the accomplishment of cross aldol reactions in buffered aqueous medium using nicotinic and other pyrrolidine based catalysts. Chimni et al. also reported that heteroaromatic (50) and aromatic aldehydes (50) undergo fast direct cross-aldol reactions with ketones (51) in water in the presence of a catalytic amount of pyrrolidine affording the aldol addition product (52a, 52b, 54a, 54b) in 93% yield (Scheme 17, 18). Since the use of water as reaction solvent has many positive effects in terms of cost, safety, and environmental impact. However, early studies about the use of chiral organic catalysts in aqueous medium met with only limited success. Only very recently Barbas and Hayashi reported very efficient proline-derived chiral catalysts for the aldol condensation “in water”. Other examples of organocatalysts developed for stereoselective reactions in aqueous solvent were tryptophan, small peptides, pyrrolidine-based catalysts, or proline-related systems. Guizzetti et al. reported the direct aldol condensation of cyclohexanone and other ketones (51) with different aldehydes (50) in the presence of a massive amount of water by using 1,1'-Binaphthyl-2,2'-diamine-based (S)-prolinamides in the presence of stearic acid affording aldol products (55) with very good yields, high diastereoselectivity, and up to 99% ee (Scheme 19). From the literature survey, it is known that aldol reaction in aqueous media usually require Lewis acid activation of the acceptors and the use of silylenol ethers as aldol donors catalyzed by a good small organic-molecule catalyst. In one case, aldol reactions were also catalyzed by a proline-like molecule in a buffer solution with 10% DMSO. Peng et al. investigated environmentally benign Aldol reactions of ketones (51) with nitrobenzaldehydes (56) in aqueous SDS micelle affording product (57) (Scheme 20).



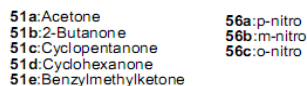
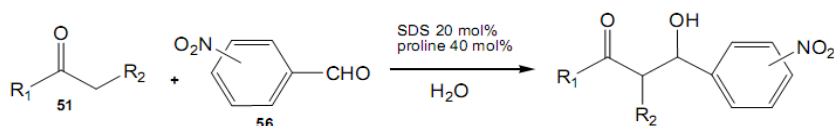
Scheme 17



Scheme 18



Scheme 19



Scheme 20

Xing et al. reported a simple environmentally benign and efficient method for the asymmetric synthesis of chiral 3-allyl isoindolinone compounds by treating 2-formylbenzoate imine (58) with indium (60) and allyl bromide (59) in saturated aqueous NaBr affording products (61) with excellent diastereoselectivities (>99:1 dr)

CONCLUSION:

Green Chemistry is a concept for scientists envisioned by scientists for higher efficiency, not a mandate or a condemnation from outside of the scientific community. In short, Green Chemistry is neither a new type of chemistry nor an environmental movement, a condemnation of industry, new technology, or "what we do already". Green Chemistry is simply a new environmental priority when accomplishing the science already being performed regardless of the scientific discipline or the techniques applied. Green Chemistry is a concept driven by efficiency coupled to environmental responsibility. Green Chemistry philosophy provides a design for chemical evolution and a guide for scientists to accomplish sustainable practices during chemical research, development, and manufacturing. It has been proposed that evolution toward Green Chemistry has recently crested a summit²⁵ and gained momentum enough that general technical exemplification is both imminent and inevitable. Clearly, scientist better recognize and acknowledge the need for greater synthetic efficiency and environmental concern. Unfortunately, the scientific community as a whole has yet to commit the necessary resources to enable this higher level of efficiency through greener chemistry. What has been accomplished is a sea change in the attitude of many academic and industrial scientists, and a wide acceptance that the philosophy of Green Chemistry offers great potential economically and environmentally. Green Chemistry insists that our synthetic objectives are achieved while assuming additional considerations related to the unnecessary environmental burden created during operations. If using a toxic reagent, one should inquire if a less toxic reagent might accomplish similar ends. A literature search may provide no current alternative with similar efficiency and reduced toxicity, but many do not realize that the simple act of inquiry toward reduced toxicity already indicates a new priority and intent, a higher level of awareness and environmental stewardship, and is Green Chemistry! In some cases a safer reagent will exist. Application will improve the process environmental profile and reduce risk related to working with a toxic reagent while maintaining or improving synthetic efficiency. Some believe an environmental priority will add time and cost. Just the opposite, time and cost are reduced by incorporating higher synthetic efficiency the first time, and new methods can be applied toward parallel and future endeavours to enhance overall productivity.

REFERENCES

- [1] Anastas, P.T.; Warner, J. Green Chemistry: Theory and Practice, Oxford University Press: Oxford, 1988.
- [2] Anastas, P.; Kirchoff, M.; Williamson, T. Spinosad – a new natural product for insect control. *Green Chem.*, 1999, 1, G88.
- [3] Vasilev, A.; Deligeorgiev, T.; Gadjev, N.; Kaloyanova, St.; Vaquero, J.J.; Alvarez-Builla, J.; Baeza, A.G. Novel environmentally benign procedures for the synthesis of styryl dyes. *Dyes Pigm.*, 2008, 77, 3, 550-555.
- [4] Toda, F., Schmeyers, J. Selective solid-state brominations of anilines and phenols. *Green Chem.*, 2003, 5, 701-705.
- [5] Bogdal, D.; Pielichowski, J.; Jaskot, K. Remarkable fast N-Alkylation of Azaheterocycles under microwave irradiation in dry media. *Heterocycles*, 1997, 45, 715-722.
- [6] Bogdal, D.; Pielichowski, J.; Jaskot, K. New method of N-alkylation of carbazole under microwave irradiation in dry media. *Synth. Commun.*, 1997, 27, 1553-1560.