GREEN CHEMISTRY - A NEW APPROACH IN ORGANIC SYNTHESIS

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Green chemistry is the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical product[1]. In keeping with the current trends to bridge new innovations and technologies with environmental issues, CSIR-NEIST, Jorhat has embarked on a mission to develop and promote new discoveries and inventions based on 'green chemistry' principles. Herein we present a brief report on the efforts of the NEISt scientific stuff towards green synthetic methodologies.

"Some see things as they are, and ask why. I see things as they should be and ask, why not."

Robert F. Kennedy

Chemists have always striven for efficiency in their synthetic methodologies. In doing so, the most fundamental challenge that a chemist faces is to make the substances they use as environmentally benign as possible. It is in this context that the concept of green chemistry comes in. To accomplish the goal of designing and executing an environmentally benign synthetic protocol, green chemistry provides a way out by addressing one basic environmental problem: the problem of pollution.

Tools of Green Chemistry

As the environmental and health effects of a chemical or chemical process is now ideally considered at the design stages, the approaches and the development techniques have been quite diverse. Since the types of chemicals and the types of transformations are so varied, so too are the green chemistry solutions that have been proposed. These can be broadly clubbed into a several categories.

In developing green synthetic strategies, one needs to concentrate on avoiding environmentally noncompatible reagents, solid-state synthesis and modification of synthetic routes to decrease the number of steps and increase the overall yield, usage of newer catalysts and simplification of classical procedures of reaction[1]. Catalyst and reagent chemistry is one of the most important aspects of eco-friendly chemistry. Reagent chemists are working toward development of more benign and selective reagents that require ambient conditions. The elimination of hazardous solvents is one of the prime concerns among them. Enzymes have emerges as biotechnological tools, which can offer solutions to the major problems of the chemical society. Efforts are devoted for the enhancement of an application base of enzymes to develop new alternative sweeteners such as high fructose corn syrup (HFCS), synthetic honey and other food products such as polysaccharide gums, thickeners and flavour enhancements. Analytical chemistry has been at the centre of the green chemistry movement. Advances in analytical chemistry are key to environmental protection. The focus for analytical chemistry is mainly on technologies such as solid-phase, ultrasound and microwave, supercritical fluid extraction and automated soxhlet extraction.

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Microwave Assisted/Solvent-free Organic Synthesis

In recent years, microwave assisted organic synthesis (MAOS) have developed into a popular branch of synthetic organic chemistry[2a-2c]. One of the most fundamental obstacles in developing technologies are to minimise the energy consumption and to eliminate/minimise the use of hazardous solvents. In this scenario, use of microwave energy to bring about chemical transformations is a suitable alternative, as it takes care of two very essential criteria of synthesis: minimise energy consumption required for heating and time required for the reaction[3a-3b]. Theoretical calculations have suggested that reactions with high activation energies can also be performed under microwave conditions without the use of harsh reaction conditions[4a-4b]. Moreover, solventless synthesis results in reaction rate enhancements along with differed selectivity compared to conventional conditions. Thus microwave heating coupled with dry reaction media presents a green protocol to carry out organic reactions.

Over the years, CSIR-NEIST, Jorhat has put in a conscious and continuous effort to develop microwave based technologies for generation of drug analogs[5-14]. For example, a novel method for the synthesis of biologically significant quinazoline moiety was developed via a three component reaction between 2-aminoarylketone, an aldehyde and urea[9]. The highlight of this 'green' protocol was rapid generation of the products in excellent yields under solvent- and catalyst-free conditions. Another microwave mediated method was developed by Prajapati, Barah and Gohain[6] for the synthesis of novel dihydropyrimidine derivatives in high yields under solvent free conditions via three component condensation of uracil amidine, ammonium acetate, an aldehyde in presence of acetic acid. Some of the biologically significant molecules synthesised at CSIR-NEIST, Jorhat, employing microwave irradiation and solvent-free conditions are listed bellow (Figure 1).

Reactions in Aqueous Media

Organic reactions in aqueous media have always been an attractive area for synthetic organic chemists. The development and applications of green chemistry principles have renewed the interests of scientific community worldwide towards designing of organic reactions in water. As a reaction medium, water has many advantages over common organic solvents. It is abundant, non-toxic and environment friendly[15-16]. Moreover, work up of the reaction and product separation is relatively easy. Because of these reasons, recent years have seen use of water as environmentally benign reaction media in a number of organic transformations[17a-17e].

The scientific community at CSIR-NEIST, Jorhat has significantly contributed towards developing organic reactions in aqueous media. Reactions such as Knoevanagel condensation,[18] oxidation of alcohols,[21] cyclocondensation reactions,[20] 1,2-addition reactions[19] and one-pot synthesis of biologically significant moieties have been developed at CSIR-NEIST by employing water as the reaction media. Some of these are shown in figure 2.

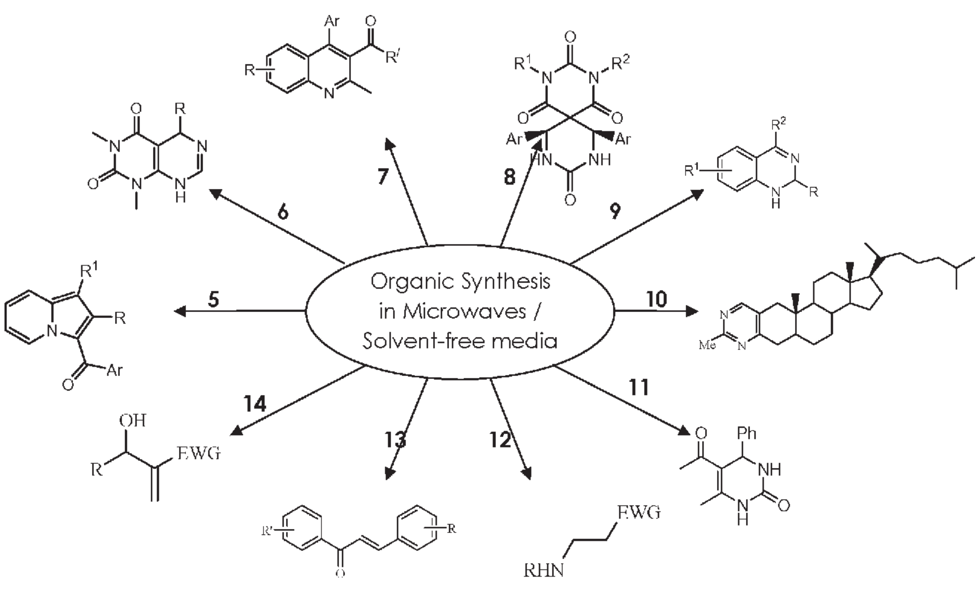


Figure 1

Enzyme Catalyzed Reaction

Enzymes are *proteins* that catalyze chemical reactions[25]. Almost all chemical reactions in a biological cell need enzymes in order to occur at rates sufficient for life. Since enzymes are selective for their substrates and speed up only a few reactions from among many possibilities, the set of enzymes made in a cell determines which metabolic pathways occur in that cell.

Like all catalysts, enzymes work by lowering

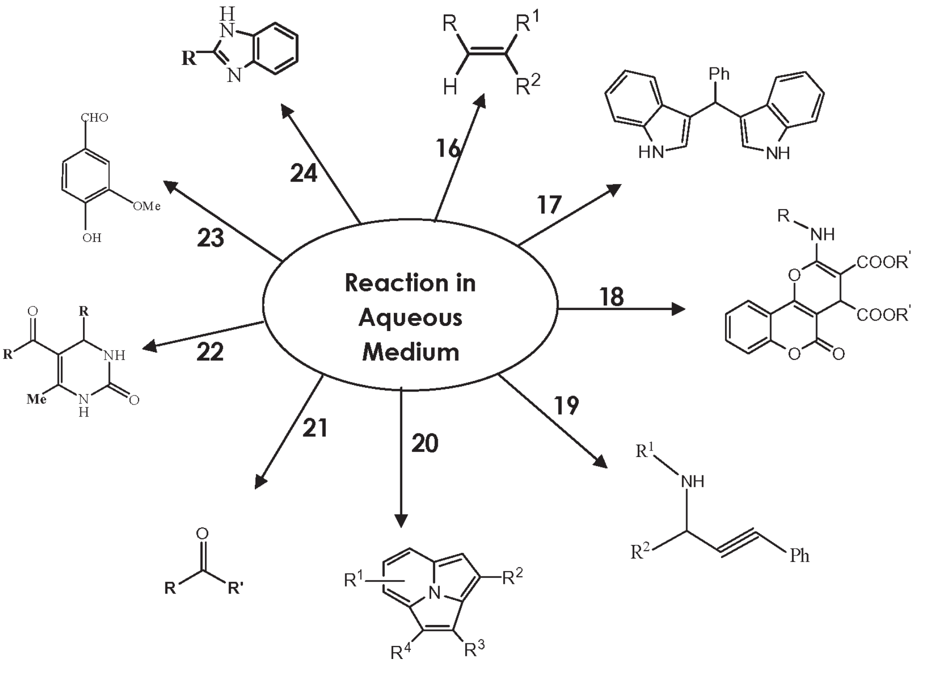


Figure 2

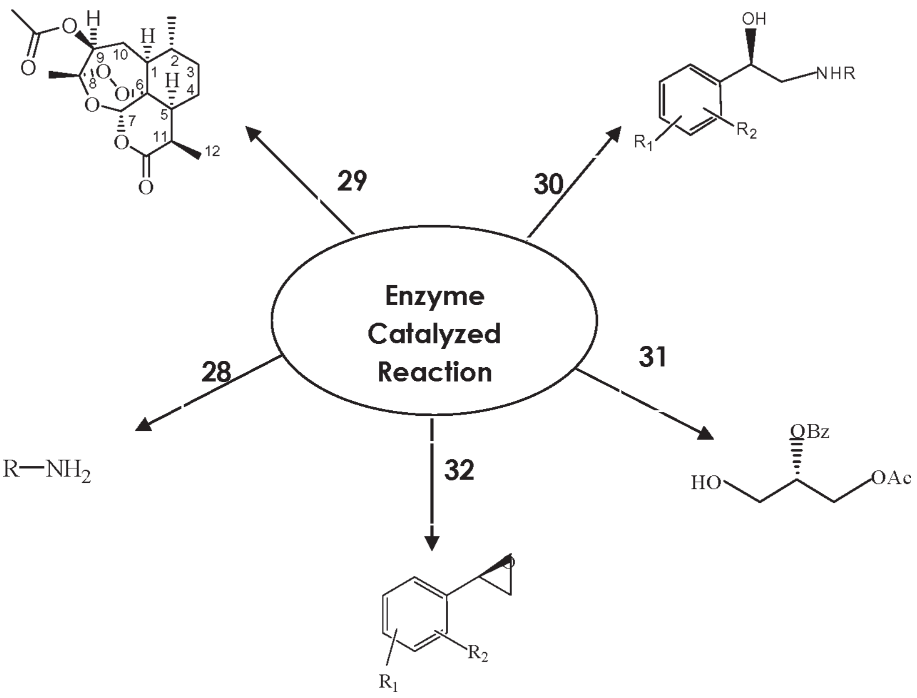


Figure 3

the activation energy for a reaction, thus dramatically increasing the rate of the reaction. As a result, products are formed faster and reactions reach their equilibrium state more rapidly. Most enzyme reaction rates are millions of times faster than those of comparable un-catalyzed reactions. As with all catalysts, enzymes are not consumed by the reactions they catalyze, nor do they alter the equilibrium of these reactions. However, enzymes do differ from most other catalysts in that they are highly specific for their substrates. Enzymes are known to catalyze about 4,000 biochemical reactions[26]. Synthetic molecules called artificial enzymes also display enzyme-like catalysis[27]. Various enzyme-catalysed reactions have been developed at CSIR-NEIST, Jorhat, for the construction of synthetically as well as biologically important units[28]. For example, the potent antimalarial compound artemisinin, was bio-transformed to C-9 acetoxy artemisinin, using soil microbe *Penicillium simplissimum* along with a C-9 hydroxy derivative.[29] Further, β-Amino alcohols that are used as β-adrenoreceptor agonists are synthesised by Goswami *et al*[30-31] from prochiral carbonyl compounds using immobilized microbe *Rhodotorula rubra* a yeast group of microbe from local municipal wastes in water at room temperature to get product with 95%-*ee*[32]. Some of the molecules synthesised at CSIR-NEIST via an enzyme catalyzed reaction are shown in figure 3.

Heterogenous Catalysis

The study of heterogeneous catalysis dates back to early 1980s. Faraday was one of the first scientists to examine the ability of platinum to facilitate oxidation reactions. Many other heterogeneous catalytic processes were subsequently developed that facilitated hydrogenation, dehydrogenation, isomerisation, and polymerisation reactions.[33] In recent times, apart from the classical reactions, the concept of heterogeneous catalysis has been applied in almost every aspect of organic synthesis.

At CSIR-NEIST, Jorhat, various groups are working in tandem to develop heterogeneous catalysts as well as for their application in organic transformations. Metal based

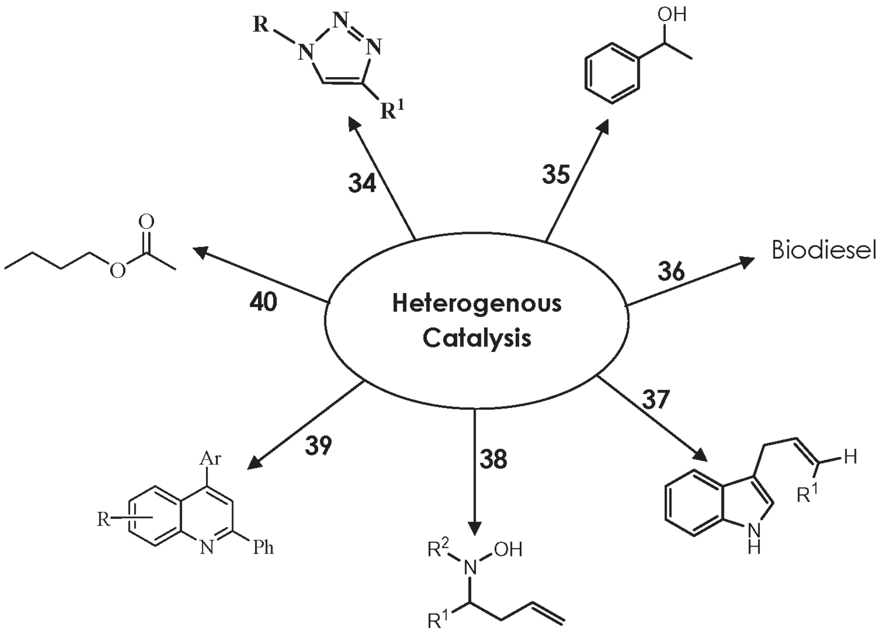
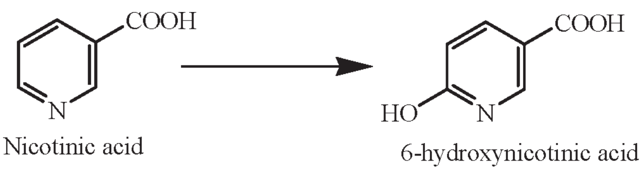


Figure 4

nanoparticles such as Cu^0- and Ni^0 nanoparticles have been synthesised and their applicability is tested for azide-alkyne cycloaddition[34] and catalytic transfer hydrogenation[35] reactions. Some examples of compounds synthesised at CSIR-NEIST, Jorhat by employing heterogeneous catalysis[36-40] as the key step in the respective organic transformations are shown below (Figure 4).

Green Technologies

The process for production of 6-hydroxynicotinic acid developed at CSIR-NEIST, Jorhat is based on enzymatic



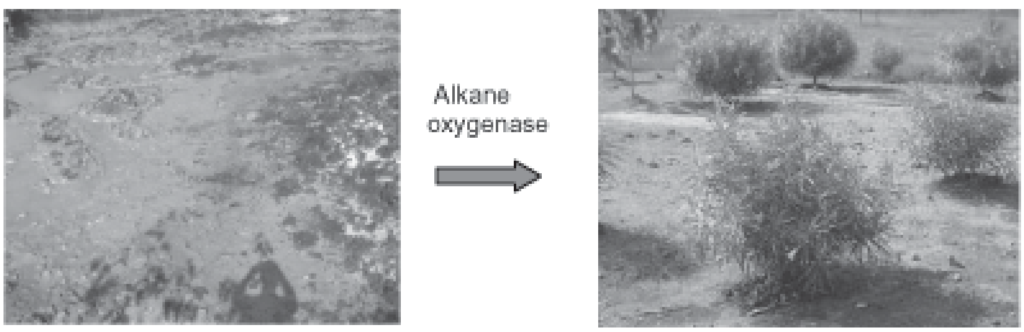
Scheme 1

hydroxylation of nicotinic acid using *Pseudomonas* sp. in a single step reaction[41]. 6-hydroxy nicotinic acid is used as a starting material for synthesis of new generation insecticides imidicloprid and medicine e.g. pyridyl-pyridazinone compounds effective for the treatment of congestive heart failure. The technology is helping as import substitute, since we had to import 6-hydroxynicotinic acid from abroad (Scheme 1).

Assam is rich in mineral oil. CSIR-NEIST-Jorhat developed a process to bring back the sites to the original condition by application of some green technology. As per the bio-chemical nature of the contaminated sites, treatment is made with microbial enzyme like Alkane oxygenase, Polyaromatic dioxygenase or any other suitable bacterial metabolites. With this technology NEIST-Jorhat already reclaimed six drill sites (each area is about 14,500 Sq M) and turned into greenery[42]. Our technology is a quick process with complete bioremediation within a period of 18-24 months with 80 to 90 % hydrocarbon contamination.

Conclusions

In conclusion, practising green chemistry have become a necessity rather than an option as this is a high time to protect our environment from further damage. The scientific community at CSIR-NEIST is pursuing research in such a way that it is beneficial for the common people as well as for the environment. The scientists are working towards developing green technologies in a diverse area such as enzyme and heterogeneous catalysis, microwave reactor mediated reaction, solid state reaction, reaction in aqueous phase etc. The practice of green chemistry is a moral responsibility for all research scholars and students. Industries should also understand their responsibility towards protecting the environment and in this regard



Area before treatments   Area after treatments government agencies should ensure strict enforcement of laws for practicing green chemistry. Green chemistry is a journey rather than a conclusion and through its continual improvement, discovery and innovation, one can hope to attain the perfect goal of designing environmentally benign technologies. ❒

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