



A Focus & Review on the Advancement of Green Chemistry

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ABSTRACT: Green chemistry which is the latest and one of the most researched topics now days has been in demand since 1990's. Majority of research in green chemistry aims to reduce the energy consumption required for the production of desired product whether it may be any drug, dyes and other chemical compounds. It aims to reduce or even eliminates the production of any harmful bi-products and maximizing the desired product without compromising with the environment. The three key developments in green chemistry include use of super critical carbon di oxide as green solvent, aqueous hydrogen peroxide as an oxidizing agent and use of hydrogen in asymmetric synthesis. It also focuses on replacing traditional methods of heating with that of modern methods of heating like microwave radiations so that carbon footprint should be reduces as low as possible. This review emphasize on principle, methodology and recent applications of green chemistry. © 2011 IGJPS. All rights reserved.

KEYWORDS: Energy; Catalyst; Precursor; Carbon Footprint.

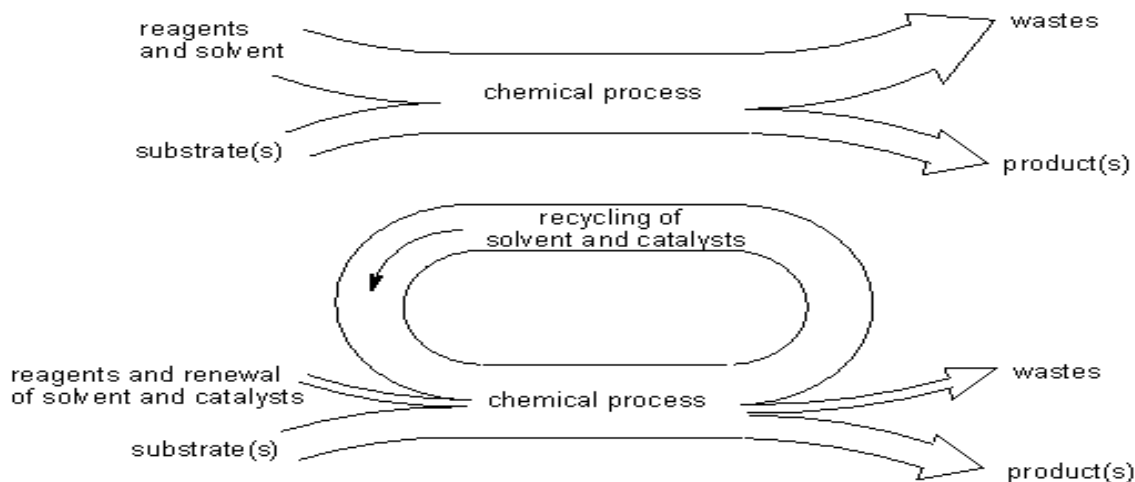
INTRODUCTION

Chemistry as a separate discipline took its shape in the beginning of 17th century also referred to as "age of reason". Since then the properties and use of different compounds has fascinated many Scientist. Many new molecules have been discovered, synthesized, studied and used. After gaining ample knowledge about the properties and uses of compounds whether organic and inorganic products, A need was generated to make these compounds available to all. So the commercial production of many of the compounds took place. A huge increase in the exploitation of petroleum and its related compounds also took place. Commercial production and mass utilization of dyes, drugs, educts, solvents etc. started and till now the use has been continued and will always be in use in future also.

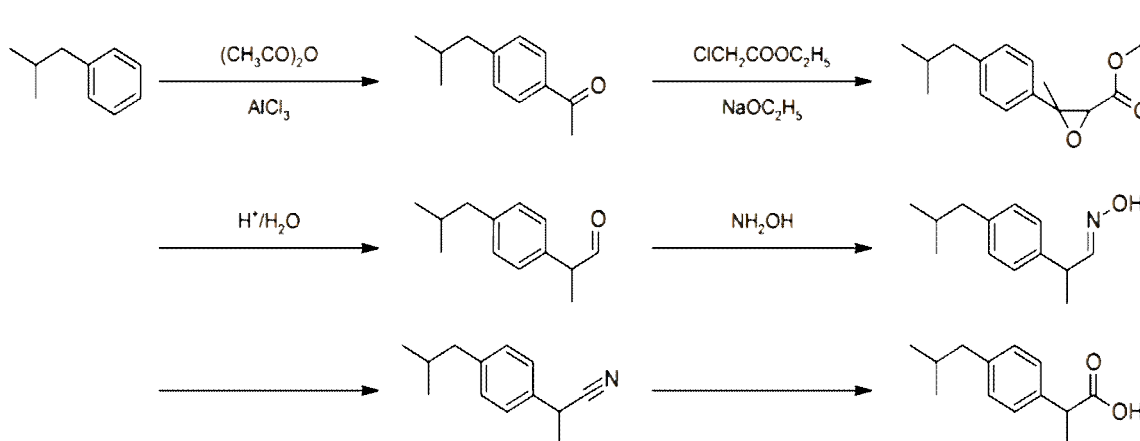
LITERATURE & DISCUSSION

Green chemistry as the name indicates is a technology imbedded, environmental friendly and cost effective utilization of resources that minimize or even eliminate the production of harmful bi-products in the design and manufacturing of the product[1]. Presence of such unwanted bi products not only lowers the yield of the desired product but may also interface with the utilization of the product.

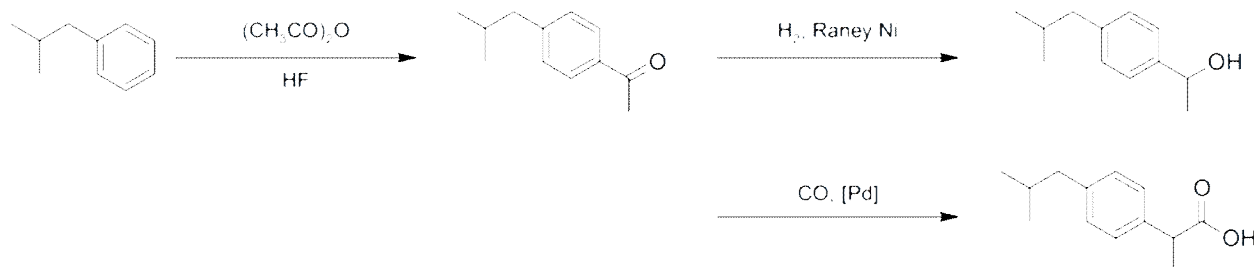
Presence of these bi-product even after the purification process limits its use. Under these prospective green chemistry aims to eliminate the production of these unwanted products and hence widens the usage of products[2].



A very important example is ibuprofen which is a non steroidal anti inflammatory drug (NSAID) which is widely used for the relief of symptoms of arthritis, constipation, fever and also exerts antiplatelet effect[3] is manufactured industrially as Classic route for the production of ibuprofen is as follows[4]:



But looking at the production of unwanted bi-products which if present even in trace amounts may hinder its pharmacological activity. A new way of production of ibuprofen which is based on the principles of “Green chemistry” eliminates the production of bi-products and also an increase in the yield has been observed[5].



This improved synthesis won the president green chemistry challenge greener synthetic pathways award in 1997[6,7].

Principles of Green Chemistry

Paul Anastas and John C. Warner put forward 12 principles of green chemistry which forms the basis of green chemistry and helps attaining following basic requirements which are[8-16]:

- a) To design and development of such processes which maximizes the conversion of raw material to products so that maximum yield of product is obtained.
- b) To implement the usage of such substances which are environment friendly or substances which are derived from environment including solvent, whenever possible.
- c) Designing of energy efficient processes.
- d) Disposal of waste material so avoided that it should not produce in the reaction or if not possible should be treated in such a way that it should not harm the environment.

The 12 principles of green chemistry are:

1. It is better to prevent waste than to treat or clean up waste after it is formed.
2. Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.
3. Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
4. Chemical products should be designed to preserve efficacy of function while reducing toxicity.
5. The use of auxiliary substances (e.g. solvents, separation agents, etc.) should be made unnecessary whenever possible and, innocuous when used.
6. Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.
7. A raw material feedstock should be renewable rather than depleting whenever technically and economically practical.
8. Unnecessary derivatization (blocking group, protection/ deprotection, temporary modification of physical/ chemical processes) should be avoided whenever possible.
9. Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
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.
11. Analytical methodologies need to be further developed to allow for real-time in-process monitoring and control prior to the formation of hazardous substances.
12. Substances and the form of a substance used in a chemical process should chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires.

Catalyst and Solvent Usage

Till now a vast variety of techniques have been designed to support and to form the basic foundation pillars of green chemistry some of them are as follows[17]:

- 1) Till now it is considered to be one of the most important characteristic of green chemistry. The main reason of using “green catalyst” is that its action mimics nature in respect that all natural synthesis is enzyme catalyzed reactions. This not only helps in designing a highly stereo specific, stereo selective and enantio- selective product but also these reactions takes place under ambient

conditions. Pd and CeO₂ are among some of the catalyst widely used in green chemistry. (nitroso) Ru-salen complex, nickel(II) complexes, N-hydroxyphthalimide (NHPI) etc are some of the recently used catalyst in green chemistry[17].

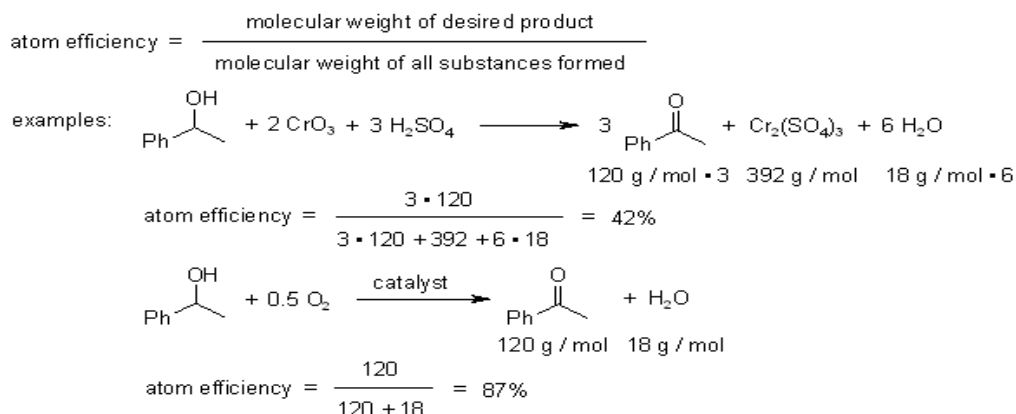
2) Generally chloroform, DMC, carbon tetra chloride etc are used as a solvent in organic synthesis which is not only costly but is very harmful for those who is handling them also. Among them carbon tetrachloride is worst solvent as it is highly environment destructive. In green chemistry an attempt has been made to minimize or eliminate these effects by using water as a solvent. Not only this super critical carbon dioxide which are obtained by elevating the temperature and pressure of the gas above its critical temperature and pressure but below the pressure required to condense it to solid. In this case CO₂ has a T_c of 304.1°K and P_c of 72.8 atm[18]. Other super critical fluids used in green chemistry are ethane, ethene, water, xenon etc. A drawback of these super critical fluids is that for organo-metallic catalyzed reactions these CSF's are too less polar to carry forward the reaction, but as compared to traditional solvents these SCF's give far better results[17].

Use of precursor materials

A great attempt has been made to shift the usage of petroleum based products which currently forms 95% of cases as a starting material for various chemicals required in tons per year. On this basis shifting to biomass for such a vast need is the call of an hour. Researchers are now finding new ways of converting biomass into starting material, which in some or the other has been a great success. E.g. converting D-glucose into lactic acid using certain enzymes helps us to prepare aliphatic compounds from lactic acid. On a similar basis E-coli converts D- glucose to catechol which acts as a starting material for aromatic compounds. On the other hand isomaltulose which is widely available in biomass can be converted into glucosylmethyl furfural which can be used for production of many heterocyclic compounds. Besides biomass cash crops is a new hope as ethanol from sugarcane has been derived successfully and now scientists are trying to use this "bio alcohol" as a source of vehicle for future. Exhaust from Corn plant has been successfully utilized for preparing bio-degradable plastic[17].

Atom based synthesis

In a chemical reaction the major concern is the percent yield of desired product. If the yield in a chemical reaction is satisfactory we hardly bother about the formation of bi-products. An attempt has been made to further maximize the yield of the desired products by developing such reactions which are catalyzed reactions whose catalyst can be extracted and further utilized for other reactions. These reactions are further focused to undergo addition reactions, rearrangements or pericyclic reaction where a single product is obtained which further increases the atom efficiency. Atom efficiency can be calculated by dividing the molecular weight of desired product to the molecular weight of all substance formed. This can be further understood by the following example[19].



For reactions whose desired product is a chiral compound, it is advisory to design such reactions which eliminates the formation of racemic mixtures. Hence these type of synthesis should always be either highly stereo-specific or either highly stereo-selective.

Effect of carbon footprint

It is a point of concern that about 1/7th of the total energy production (including electricity, petroleum and its related products, coal, and wood) are utilized in the production of chemicals by industries. Which is not only a large share of energy consumption but plays a big role in environment related hazards including global warming. Here green chemistry can play a major role in reducing carbon footprint. Minimizing the energy requirements of industries by maximizing the efficiency of chemical conversion and decreasing the activation energy of the reactions by using recyclable catalysts can cut off the energy requirement of industries by half or even more.

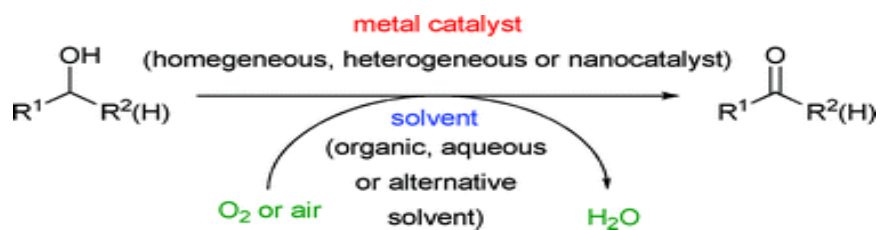
Eliminating the use of energy consuming steps like distillation, crystallization, sublimation, ultra filtration etc. and incorporation of microwave energy which aims to achieve a high temperature at much faster rates and also utilization of ultrasonic energy for certain reaction can eventually solve this problem[17].

Besides the above mentioned “pillars of green chemistry” some other points that can also be incorporated as the supports of green chemistry are as follows[17]:

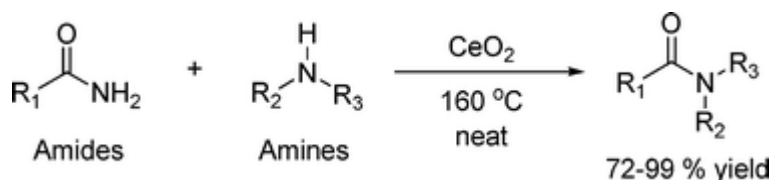
- Use of “light” as a carrier of electrons which can eventually reduce the usage of other chemical agents which act as a carrier of electron and is obtained as waste products at the end of a redox reaction.
- Eliminating the un-necessary use of protection- deprotection methodologies.
- Replacement of soluble Lewis acids by mesoporous solids containing bound sulphonates in green synthesis.
- Utilization of milder reaction conditions for carrying out a chemical reaction.

Recent advantages of green chemistry

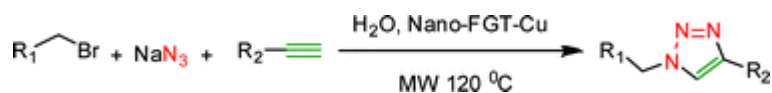
1) Oxidation of alcohol to corresponding carbonyl compounds using oxygen or even better air as stereomeric oxidants. Using this method only water is been produced as a bi-product. This reaction involves utilization of transition metals as catalyst in the form of either homogenous catalyst, Heterogenous catalyst or even better nano catalyst[20].



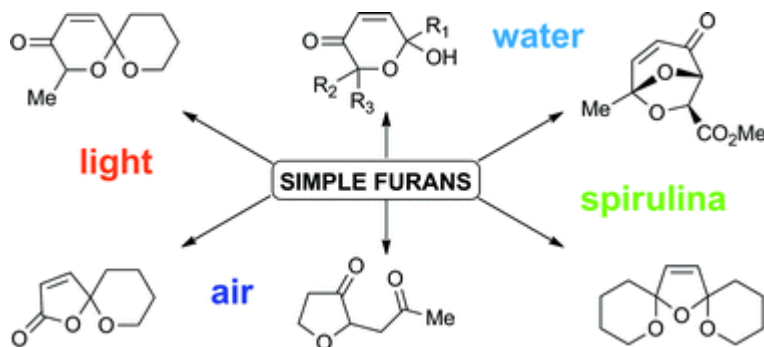
2) For transamidation of picolinamide with *n*-octylamine, cerium oxide (CeO₂) has been used which shows highest catalytic activity. This reaction has been done under solvent free conditions[20].



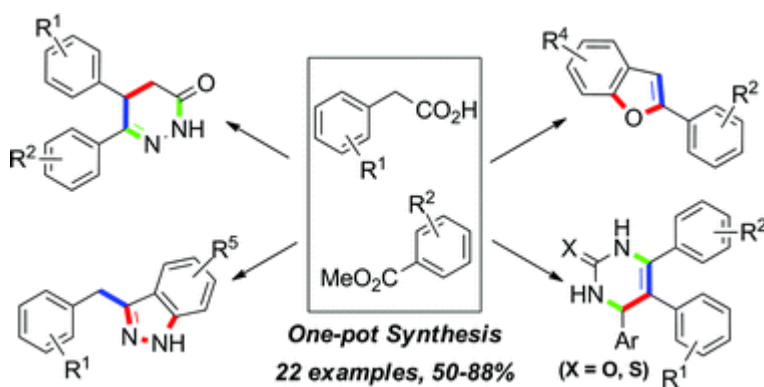
3) 1,2,3-Triazoles were synthesized in water using magnetically recoverable heterogeneous Cu catalyst *via* one-pot multi component reaction using Micro Wave irradiation. Catalyst so used can be easily recovered using an external magnet which can be efficiently recycled[20].



4) A greener way of utilizing air, sun light, water and spirulina to transform readily available furan derivatives into a wide range of synthetically useful polyoxygenated compounds which are commonly found in natural products is now possible with green chemistry[20].

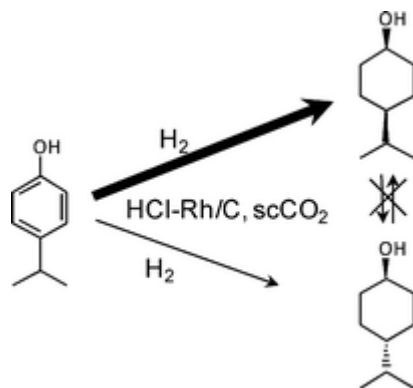


5) For synthesizing useful heterocycles in medicinal chemistry such as pyridazinones, dihydropyrimidinones, and dihydropyrimidinthiones, a “green”, mild and highly efficient one-pot triple cascade has been developed involving Claisen–decarboxylation, electrophilic reaction, and subsequent heterocyclization. In addition, indazoles and benzofurans could also be synthesized *via* a double cascade. To develop the cascade process, a direct Claisen–decarboxylation reaction was firstly optimized. This reaction was then coupled with electrophilic reactions including alkylation, Michael addition or aldol reaction to enable the preparation of various aryl ketones in a one-pot fashion[20].

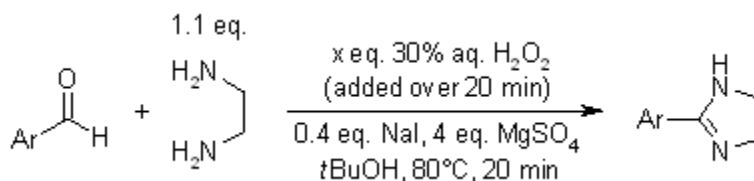


6) A study of Hydrogenation of 4-isopropylphenol to 4-isopropylcyclohexanol over activated carbon-supported rhodium catalysts in supercritical carbon dioxide (scCO₂) at 313 K in a batch reactor has been done and the results were compared with those in 2-propanol. An increase in the yields of *cis*-4-isopropylcyclohexanol were obtained in scCO₂ than in 2-propanol, and the formation of a byproduct, isopropylcyclohexane, was suppressed in scCO₂. When The catalyst was modified with hydrochloric or phosphoric acid, better yield of *cis*-4-isopropylcyclohexanol in both scCO₂ and 2-propanol solvents were observed. Kinetic analyses of these reaction profiles revealed higher reaction rates in scCO₂ than those in 2-propanol for the 4-isopropylcyclohexanol formation both by the direct

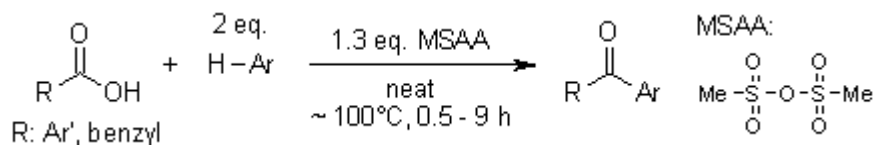
hydrogenation of 4-isopropylphenol and by the consecutive hydrogenation of 4-isopropylcyclohexanone, and also revealed that the addition of hydrochloric acid increased the consecutive hydrogenation rate of 4-isopropylcyclohexanone to *cis*-4-isopropylcyclohexanol, which reduced the total reaction time needed for the complete hydrogenation of 4-isopropylphenol to 4-isopropylcyclohexanol[20].



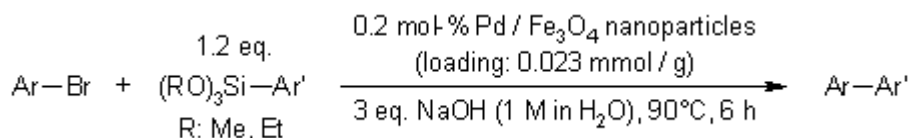
7) A new environmentally friendly, efficient and easy process for the synthesis of 2-imidazolines has been developed which aims to give a better results which can be performed by reacting aldehydes with ethylenediamine using hydrogen peroxide as an oxidant in the presence of sodium iodide and anhydrous magnesium sulfate as catalyst. Using this synthesis no production of bi-products were observed[21].



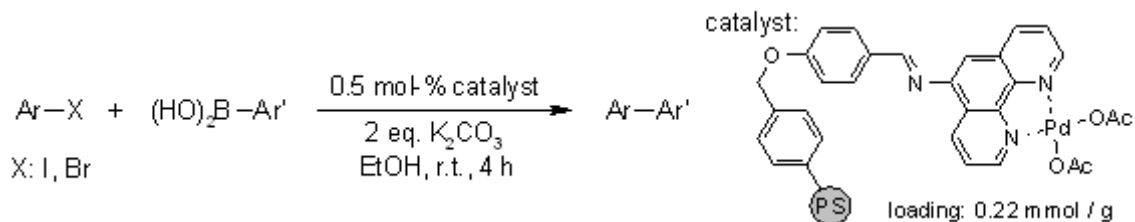
8) Now, friedel craft acylation of aryl and alkyl carboxylic acid can be done using methanesulfonic anhydride (MSAA) which allows the preparation of aryl ketones in a good yield with minimal waste containing no metallic or halogenated components, clearly differentiating it from other available methodologies[22].



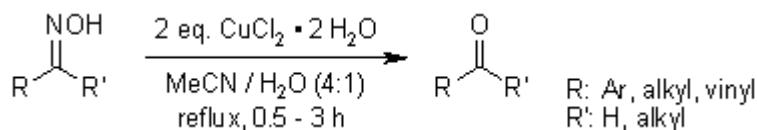
9) A new method of Hiyama Cross-Coupling was recently modified using Magnetically Recoverable Pd/Fe₃O₄-Catalyst. Cross coupling of Aryl Bromides with Aryl Siloxanes was done to yield desired product which requires comparatively less time and energy[23].



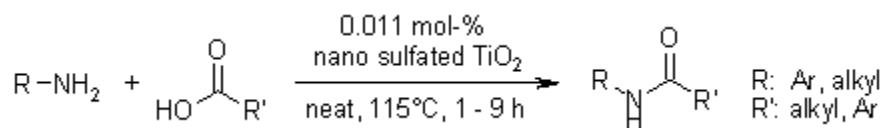
10) A new recyclable catalysts for Suzuki-Miyaura Cross-Coupling Reactions has been developed which can work at moderate Temperature. This catalyst is based on a Simple Merrifield Resin Supported Phenanthroline-Palladium (II) Complex[24].



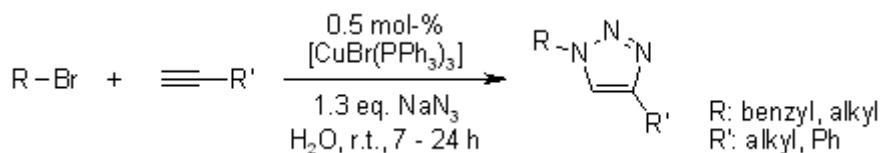
11) A new method of preparing Carbonyl compounds in very good yields has been developed. This can be done by treating oximes with 2 molar equivalent of $\text{CuCl}_2 \cdot 2 \text{H}_2\text{O}$ in the presence of acetonitrile and water in ratio 4:1 and refluxing the resulting solution for about three hours. An added advantage of recovering cupric salts can also be done in this method[25].



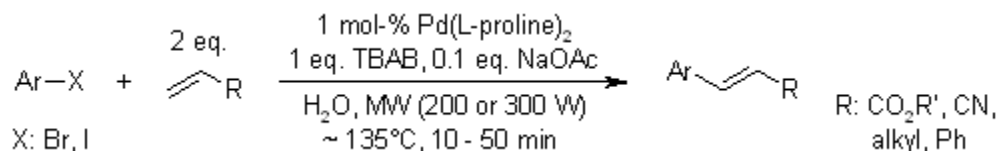
12) Nanosized sulfated titanium dioxide which was prepared by a sol-gel hydrothermal process showed high catalytic activity in a direct amidation of fatty acids as well as benzoic acids with various amines under solvent-free conditions[26].



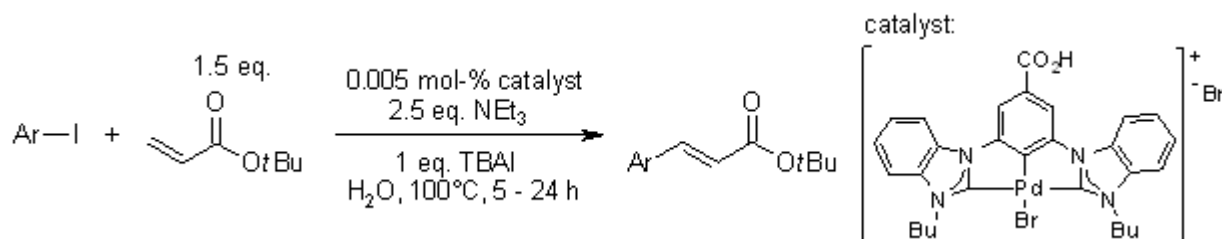
13) A new catalytic method for preparing pure triazoles has been developed which is based on commercially available $[\text{CuBr}(\text{PPh}_3)_3]$. This method do not require any special conditions, and can work ven in the absence of additive. This method does not require any purification step also[27].



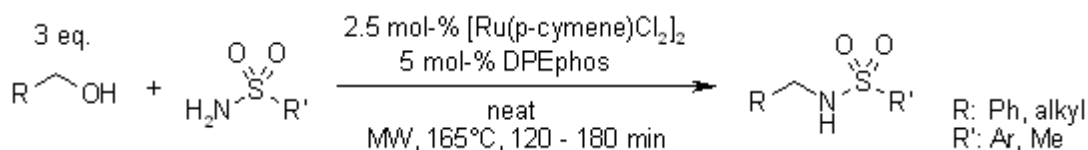
14) An efficient and simple method for “phosphine-free” Heck reactions in water in the presence of a Pd(L-proline)₂ complex as the catalyst under controlled microwave irradiation conditions is an excellent method and provides very good yields of products in short reaction times. This modified reaction system minimizes production cost, reduces operational hazards and environmental pollution[28].



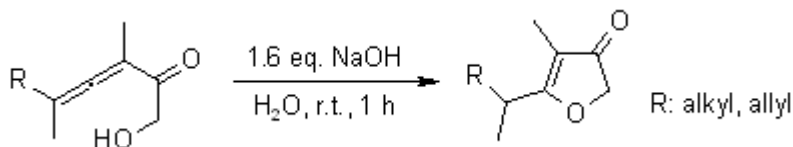
15) An Efficient Aqueous-Phase Heck Reaction which is Catalyzed by a Robust Hydrophilic Pyridine-Bridged Bisbenzimidazolylidene-Palladium Pincer Complex[29].



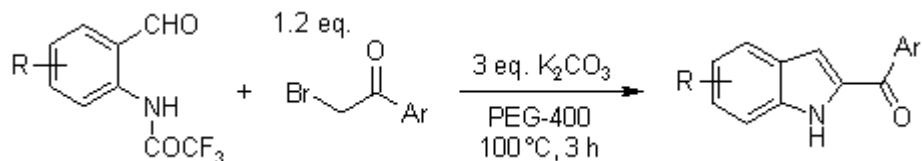
16) Replacing conventional thermal reating methods with Microwave heating enables a Borrowing Hydrogen strategy to form C-N bonds from alcohols and amines. It also eliminates the need for solvent and reduces the reaction times, while the results are comparable with those using conventional thermal heating methods[30].



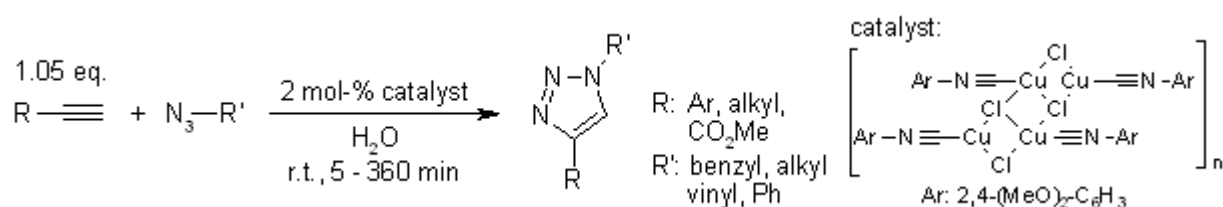
17) A simple, cost efficient and effective method of synthesis of 3(2H)-furanones by cycloisomerization of allenic hydroxyketones has been carried out in water. This method eliminates the use of any expensive metal catalyst[31].



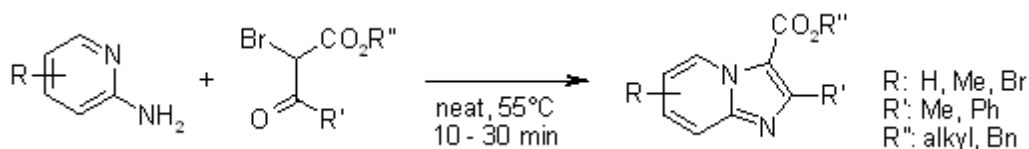
18) A simple method for the production of 3-unsubstituted 2-arylindoles using *N*-(2-formylphenyl)trifluoroacetamides and α -bromoacetophenones as starting materials in the presence of K_2CO_3 and PEG-400 as an efficient and reusable solvent enables a one-pot and environmentally friendly method for the production[32].



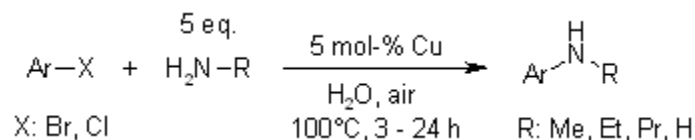
19) Copper(I) isonitrile complex has been found to be an efficient heterogeneous catalyst for azide-alkyne 1,3-dipolar cycloadditions and three-component reactions of halides, sodium azide and alkynes to form 1,4-disubstituted 1,2,3-triazoles in high yields under mild conditions in water[33].



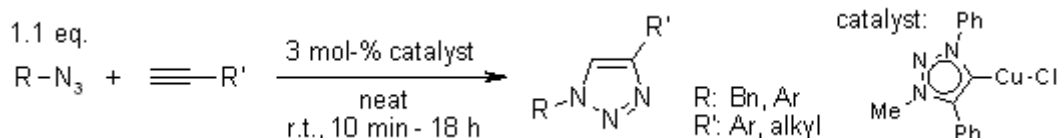
20) Temperature Controlled microwave heating of aminopyridines and α -bromo- β -keto esters has been used for the synthesis of highly substituted imidazo[1,2-*a*]pyridines under solvent-free conditions. This method gives the highest yields of products in reaction times of less than two minutes compared to the traditional way of heating i.e. thermal heating[34].



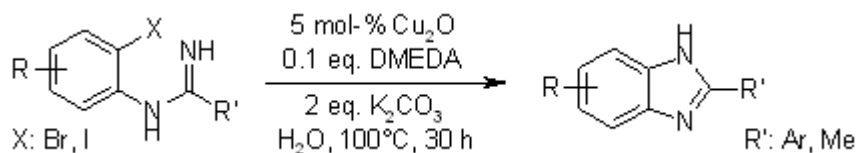
21) A new, easily friendly and practical method for Ullmann amination of aryl halides with aqueous methylamine and other aliphatic primary amines under organic solvent- and ligand-free condition at 100°C using powdered copper as catalyst in air gives a very good yield of *N*-arylamines as main products. The presence of a small amount of air is essential. This method is not suitable with Secondary amines and aniline as they do not react under these conditions[35].



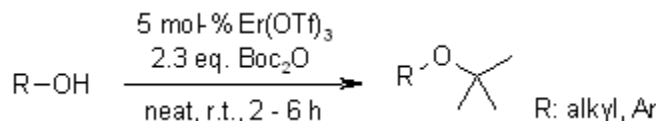
22) An abnormal NHC complex of copper with 1,4-diphenyl-1,2,3-triazol-5-ylidene [CuCl(TPh)] efficiently catalyzed click reactions of azides with alkynes to give 1,4-substituted 1,2,3-triazoles in excellent yields at room temperature with short reaction times. CuCl(TPh) was particularly effective for the reaction between sterically hindered azides and alkynes[36].



23) A straightforward, efficient, and sustainable method for intramolecular *N*-arylation yields a variety of substituted benzimidazoles in high yields using Cu_2O as the catalyst, DMEDA as the ligand, and K_2CO_3 as the base. Remarkably, the reaction was exclusively carried out in water, rendering the methodology highly valuable from both environmental and economical points of view[37].



24) An eco-compatible method for the formation of *tert*-butyl ethers of alcohols and phenols is performed in solvent-free conditions at room temperature using catalytic amount of $Er(OTf)_3$. The catalyst is easily recovered and reused several times without loss of activity. In addition, the *tert*-butyl group is removed very quickly from alcohols and phenols in methanol in the presence of $Er(OTf)_3$ using MW irradiation[38].



25) Used and exhausted vegetable oil has been used currently by researchers as a fuel for vehicles by making very less modifications in the cars of present use and a shocking result was found that by using vegetable oil CO_2 emission has been reduced to almost 67% without compromising with the efficiency of the vehicle.

CONCLUSION

It is clear that Green chemistry not only helps us in designing of new ways to synthesize the desired product economically, user friendly and it also helps to save the environment. A good flow of knowledge between the Industries and research institutions/ universities undergoing such types of research topics will not only enable us to expand our knowledge but it would also help to protect the environment. Government should also make some strict rules in governing the industries to use eco-friendly ways of production⁽²⁹⁾. It may be incorporated in the syllabus of U.G and P.G programme about green chemistry to educate young students.

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