

**STUDY AND DEVELOPMENT OF “RECYCLABLE AND
REUSABLE SILICA BASED ORGANIC - INORGANIC
HYBRID CATALYST” A CONCEPT OF GREEN CHEMISTRY**

By

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Submitted



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**STUDY AND DEVELOPMENT OF “RECYCLABLE AND
REUSABLE SILICA BASED ORGANIC - INORGANIC
HYBRID CATALYST” A CONCEPT OF GREEN
CHEMISTRY**



Dedicated to my parents

DECLARATION

“I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which has been accepted for the award of any other degree or diploma of the university or other institute of higher learning, except where due acknowledgment has been made in the text.



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Mallika Mishra

EXECUTIVE SUMMARY

In summary, we have developed a silica based organic-inorganic hybrid copper catalyst ($\text{SiO}_2@\text{APTES}@2\text{HAP-Cu}$) of unprecedented activity and recyclability through the covalent immobilization of 2-hydroxyacetophenone on the surface of the amine functionalized silica support followed by its metallation with copper chloride. The resultant heterogeneous catalytic system exhibits remarkable efficiency in terms of excellent product yield and high turn-over number in the synthesis of 1,4 disubstituted 1,2,3 triazole derivatives. The hot filtration test ensures that the catalyst works in a heterogeneous manner and is devoid of leaching problem.

Copper complex was covalently anchored onto the surface of amine functionalized silica gel, and its catalytic efficacy was investigated for oxidative homocoupling of terminal alkynes. The features of mild reaction conditions, simple work-up procedure, excellent product yield, high turn-over frequency (TOF), easy recovery and reusability of the catalyst are the significant advantages of the present protocol.

In two of the largest generic areas of chemistry, acid catalysis and partial oxidations, there are countless processes operated by almost every type of chemical manufacturing company, producing products of incalculable value yet also producing almost immeasurable volumes of hazardous waste. The enormous range of reactions and the rapidly growing number of new catalysts will require the use of rapid screening methods and the use of innovative

engineering to fully exploit the new chemistry. In the future, the synthetic chemist will need to be as concerned about atom efficiency as the synthetic route and the process chemist will need to be as concerned about the waste produced as the product to be made. Most of the reported copper catalyzed systems are associated with numerous shortcomings such as low product yield, prolonged reaction time, complicated product separation, difficult catalyst recycling and product contamination caused by the residual components of the catalysts.

It is very easy to modify silica gel with wide variety of functional groups, due to this property it can be use in numerous application, some of them are preparation of fine and speciality chemicals and pharmaceutical compounds. In this research, an attempt will be made to prepare a novel efficient and reusable metal based catalyst we will designed various sustainable silica supported organic-inorganic hybrid catalysts, which by its efficiency, recoverability and selectivity, enhance chemical transformations and contributes to the environment friendly chemical processes. Within this framework, we have synthesized several silica based organic-inorganic hybrid catalysts and investigated their catalytic efficacy in various organic transformations. The synthesis of silica based organic-inorganic hybrid copper catalyst and its application in the oxidative homocoupling of terminal alkynes. Thus, many efforts have been paid to the development of efficient and selective methods for the synthesis of diyne derivatives.

ABBREVIATIONS

SPME: - Solid Phase Micro-Extraction

SPE: - Solid Phase Extraction

ASE: - Accelerated Solvent Extraction

TGA: - Thermo Gravimetric Analysis

APTES: - 3-Aminopropyl triethoxy silane

TEM: - Transmission electron microscopy

SEM: - Scanning Electron Microscope

FT-IR: - Fourier transform infrared spectroscopy

VSM: - Value-Stream Mapping

EDS: - Energy Dispersive Spectrometer

X-RD: - X-ray Diffraction

NMR: - Nuclear Magnetic Resonance

CPMAS: - Cross Polarization Magic Angle Spinning

DMSO: - Dimethyl sulfoxide

THF: - Tetrahydrofuran

DMF: - Dimethylformamide

DCM: - Di-chloromethane

BET: - Brunauer–Emmett–Teller

AAS: - Atomic absorption spectroscopy

2HAP: - 2-hydroxyacetophenone

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CHAPTER 1

INTRODUCTION

1. INTRODUCTION

For the production of fine chemicals much attention has recently been directed towards the development of clean and green catalytic methodologies due to increasing economical pressures and environmental standards. Selectivity, good activity and high turnover number are the major advantages of homogeneous catalyst. Due to this reason they are mostly used for various organic transformation, but difficulty was found in separation of these soluble catalysts from reaction mixture, especially for expensive and toxic heavy metal complex. In the pharmaceutical industry as metal contamination is highly regulated so, it is necessary to remove hazardous toxic metals from the product. Most significant features for many green synthetic methods are catalyst recovery and its reuse.

Recently, several attempts have been made in this direction amongst which heterogenization of existing homogeneous catalysts represents a logical approach. All the demerits associated with homogenous catalysis could be overcome by converting the homogenous catalyst to heterogeneous catalyst and the process can be converted to a more desirable and clean one. Moreover, enhanced catalyst stability within the polymer support, increased selectivity, simplicity in handling toxic materials and facile work up procedure are other important benefits gained as a result of immobilization. There have been numerous reports in the literature wherein materials like zeolite, clay, activated charcoal, sand, polymers, and

highly dispersed silica have been employed as solid support in order to address the recyclabilities of the transition metal based catalyst whilst keeping their performances. Due to many advantageous properties of silica gel such as high mass exchange characteristics, great resistance to organic solvents, relatively simple covalent modification with organic or organometallic moieties, easy availability and inexpensiveness among various solid supports, silica gel is usually preferred. Simplest routes to produce heterogenized catalysts is physisorption of catalytic active species onto silica gel, but there occur leaching of the active component into the reaction mixture and from an industrial perspective which is a serious problem. Grafting of active species onto silica gel is usually done by means of covalent linkage to circumvent this problem of leaching.

Within this framework, the catalytic efficacy of silica based copper catalyst was evaluated for green oxidative homocoupling of terminal alkynes. 1,3-Diynes widely occur in numerous bioactive compounds, natural and pharmaceutical products, which possess prominent biological activities such as anti-HIV, anti-inflammatory, antifungal, antimicrobial, antitumor, anticancer and antibacterial properties. Apart from this, they also play an important role in the design of advanced materials such as conjugated polymers, liquid crystals and molecular wires. Thus, many efforts have been paid to the development of efficient and selective methods for the synthesis of diyne derivatives. The most imperative route reported in the literature for the preparation of symmetrical diynes is the palladium catalyzed homocoupling reaction of terminal alkynes owing to its

mildness, selectivity and efficiency. However, these palladium catalysts are expensive and often require air-sensitive and expensive phosphine as well as foul-smelling amine reagents. As per Glaser, copper catalytic system has been active due to their easy availability, non-toxicity, facile handling and low cost for homocoupling reaction of terminal alkynes in 1869. Most of the reported copper catalyzed systems are associated with numerous shortcomings such as low product yield, prolonged reaction time, complicated product separation, difficult catalyst recycling and product contamination caused by the residual components of the catalysts. A few efficient catalytic systems for the heterogeneously copper catalyzed alkyne homocoupling reactions have been reported which also exhibited some limitations for example large amounts of catalyst, high temperature and high pressure. Thus, there is still a major challenge to develop new recoverable catalytic systems for oxidative homocoupling of terminal alkynes under mild reaction conditions.

This study about elements, atoms, molecules, chemical reactions and other concepts essential to understand the science of chemistry. Anybody interested in green chemistry clearly wants to know how chemistry affects people all around the world.

Green chemistry effectively utilizes raw materials, eliminates waste, use renewable feedstock, catalysts and avoids the use of toxic and/or hazardous reagents and solvents in the manufacture and application of chemical products.

The design and synthesis of novel catalysts for organic transformations that are inherently environmentally and ecologically benign is a challenging task in development of chemical processes. Homogeneous catalysis offers milder reaction conditions, better selectivity and activity so they are considered to be one of the most proficient and environmentally sustainable routes to synthesize high added-value chemicals. Applications of different homogeneous catalysts in industrial processes are however hindered by their high costs as well as difficulties in separation of the catalyst from the reaction mixture. Heterogenization of homogeneous catalysts represents a logical approach to overcome those problems. Solid catalysts which are easily reusable and recyclable are provided potentially by heterogenized catalysts that have uniform and precisely engineered active sites similar to those of their homogeneous counterparts, and therefore combine best attributes of both homogeneous and heterogeneous systems. In fact, the last decade has witnessed an emerging attention in the development of organic-inorganic hybrid catalysts employing various support materials such as alumina, silica, clay, activated charcoal, zeolite, and polymers. Among various solid supports, silica gel is usually preferred due to its various inherent properties.

Within this framework, we have synthesized several silica based organic-inorganic hybrid catalysts and investigated their catalytic efficacy in various organic transformations. In our ongoing research work on the design and synthesis of silica based organic-inorganic hybrid materials and their applications

as metal scavengers, sensors, and catalysts for various organic transformations reactions herein, we report the synthesis of silica based organic-inorganic hybrid copper catalyst and its application in the oxidative homocoupling of terminal alkynes. The intrinsic stability, excellent product yield, ease of recovery and mild reaction condition of the catalyst make this methodology economical and sustainable.

To extract, purify and to dissolve reactants solvents are used. These solvents usually recycled, for economic reasons. Unfortunately many organic solvents are volatile, flammable and may cause a risk to health and environment. In atmosphere vapour cannot be exhausted therefore, all trace of these solvents must be captured separately.

A different approach is also developed, and one with growing areas of application is the use of supercritical fluids, of which the most common is carbon dioxide.

In last 200 years chemistry has made numbers of useful products and materials, and improved our life quality. But this comes at price for: non-renewable natural resources and global environment. To restores the planet's sustainable development green chemistry and its principle want to change all these negative impacts and through design, innovation and green processes. A typical example is use of non-renewable fossil fuels. As the primary building block to create chemicals, chemical industry relies almost entirely on petroleum. Such chemical production generally is very energy intensive, toxic and inefficient, resulting in significant energy use, and generation of hazardous waste. Use of alternative and

renewable materials is one of the principles of green chemistry including the use of agricultural waste or biomass and non-food-related bio products.

Green chemistry, the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances, is an overarching approach that is applicable to all aspects of chemistry. Green chemistry dynamically explores ways to generate materials which are more significant to human health and environment itself. Whether, it is by modification to solvents, to synthesis and processing. Green chemistry contains the meaning of radical change, innovation, rejection of old attitudes and practices so its name was changed from sustainable chemistry to green chemistry.

Green chemistry introduced the principles of energy efficiency, atom economy in chemical processes with reduction of waste and also promoted safer chemicals and protection of the environment. Green chemistry is a way of dealing with risk reduction and pollution prevention by addressing the intrinsic hazards of substances. In industry, chemical waste reduction is also a part of green change due to higher environmental taxes. Green Chemistry gives great importance to the term “hazardous” for processes and life cycle of chemical substances. From the standpoint of the atom economy, reactions such as addition and rearrangement reactions are inherently atom economical which is likely to produce less waste than other reactions. When devising a synthetic strategy such reaction types are worth full.

Green chemistry is very old branch of science. It is a new philosophical approach that sustainable development can be achieved through augmentation and use of the principles of green chemistry. Now a day's there are many interesting examples which are using rules of green chemistry. They are used not only in designing, generating and application of chemical compounds but also govern many analytical methodologies realized. These rules of green chemistry also useful in proceeding various chemical processes and in estimation of these process effects on environment. Use of appropriate sample preparation method, (e.g. SPME, SPE, ASE) allows (help) us to find accurate and precise results of sample analysis. To introduce an ideal process which leads to no secondary products but starts from non-polluting initial materials, great efforts are still going on. That designed process compels no solvents to perform the chemicals transformation or to isolation and purification of the products. However, there is no guarantee that the environmentally friendly technologies which are now at research stage will be implemented on industrial scale. Higher flexibility in regulations, new programs that facilitate technology transfer among institutions, government and industry along with tax incentives for implementing cleaner technologies may be adopted to facilitate environmentally benign methods.

CHAPTER 2:

SCOPE OF THESIS

CHAPTER 2

SCOPE OF THESIS

2.1 SCOPE OF THESIS

The work of green chemistry is based upon environmental chemistry. This branch of chemical science includes study of sources, reactions, effects, Study of the sources, reactions, effects, and consequences of chemical species in living environments, water, air and soil.

Green Chemistry is termed as invention, method, evaluation and application of chemical products that can prevent or minimize waste and the processes to eliminate the use and generation of products harmful to human health and environment.

A central driver in advancement of green chemistry is its economic benefits. After application of green chemistry a wide range of operating costs is reduced and even many industries are also adopting methodologies of green chemistry due to improvement in corporate bottom line. When generation of waste is less then treatment and disposal of waste become unnecessary and automatically environment compliance cost go down.

Green Chemistry aims not only for safer substances, less hazardous results to the environment, saving water and energy, but also involve issues that can elevate Sustainable Development. Two revolutionary fields with significant overlap are sustainable agriculture and green chemistry although their connections are not developed and also not appreciated. The production of hydrocarbons from Fischer-Tropsch reaction occurs using a heterogeneous catalyst typically composed of iron, cobalt, or ruthenium as the active catalyst supported on an inert oxide such as silica, titania, or alumina. For controlling and creating texture and porosity of a silica catalyst support a unique method is provided by sol-gel derived silica. The three dimensional structure and porosity properties of silica aerogel impart certain advantages over traditional oxide supports. And in addition the metal particle is effectively locked into position, if the pore size of support is smaller than metal particle size. This should allow for catalytic reactions to take place at high temperature without the risk of sintering the catalyst.

The goal of green chemistry is to reduce energy, material, and waste as well as to decrease risks and hazards in production processes. Due to contribution in sustainable development in environment and significance on economic consideration they are selected.

2.2 PURPOSE

Main aim of green chemistry is to use solvents and chemicals which are safer, design synthetic method which is less hazardous and use safer reaction condition and to reduce risk in laboratory. Separation of product/catalyst from the reaction

mixture is the major contributors to waste in a chemical process. Large volumes of waste effluent (typically salts and contaminated aqueous streams) generates in this process. Also, sometimes catalyst can destroyed during the process of extracting the catalyst. Thus, elimination of this step would be favourable and is one of the major goals of green chemistry.

In other way we can say to minimizing the environmental footprint, reduce the use of chemical derivatives, waste minimization and prevention, taking advantage of chemicals designed for degradation, use of renewable feedstock, use of catalysts instead of stoichiometric quantities, encourage energy efficiency and controls for pollution prevention.

Surface of silica contains two types of functional groups, siloxane (Si–O–Si) and silanol (Si–OH). Thus, modification in silica gel can occur *via* the reaction of a particular molecule which either the silanol (direct reaction with the hydroxyl group) or siloxane (nucleophilic substitution at the Si) functions, although it is generally accepted that main modification pathway is reaction with the silanol function.

In this research, an attempt will be made to prepare a novel efficient and reusable metal based catalyst we will designed various sustainable silica supported organic-inorganic hybrid catalysts, which by its efficiency, recoverability and selectivity, enhance chemical transformations and contributes to the environment friendly chemical processes. Silica supported organic-inorganic hybrid catalysts can be designed by using the advantages of heterogeneous catalysts, and due to its properties of recoverability, efficiency and selectivity, it contributes to the

environment friendly chemical processes and enhance chemical transformations. Where an organic molecule is covalently bind to the surface of an inorganic support material so-called hybrid organic – inorganic catalysts, that is an approach for the immobilization of molecular homogeneous catalysts.

2.3 RESEARCH OVERVIEW

The drive towards clean technology in the chemical industry and the emergence of green chemistry related issues in chemical research and education are unlikely to be short term ‘fashions’. In the future, the synthetic chemist will need to be as concerned about atom efficiency as the synthetic route and the process chemist will need to be as concerned about the waste produced as the product to be made. More successful chemical manufacturing companies of the future will be those that can exploit the economic, legislative and public image advantages that a clean technology approach to chemical manufacturing can provide. Due to high surface area, not prone to swelling and high chemical and thermal stabilities modified silica gels exhibit advantages over modified resins. It is very easy to modify silica gel with wide variety of functional groups, due to this property, it can be use in numerous application, some of them are preparation of fine and speciality chemicals and pharmaceutical compounds in liquid phase reaction. It is in these areas where environmentally unacceptable reagents and catalysts have most widely been applied and where current manufacturing processes lead to unacceptable levels of waste

Table 2.1: Largest processes based on heterogeneous catalysis.

Reaction	Catalyst
Catalytic cracking of crude oil	Zeolites
Hydrotreating of crude oil (sulfidic form)	Co–Mo, Ni–Mo, Ni–W
Reforming of naphtha (to gasoline)	Pt, Pt–Re, Pt–Ir
Alkylation	H ₂ SO ₄ , HF, solid acids
Polymerization of ethylene, propylene, a.o.	Cr, TiCl _x /MgCl ₂
Ethylene epoxidation to ethylene oxide	Ag
Vinyl chloride (ethylene + Cl ₂)	Cu (as chloride)
Steam reforming of methane to	CO + H ₂ Ni
Water-gas shift reaction Fe (oxide),	Cu–ZnO
Methanation	Ni
Ammonia synthesis	Fe
Ammonia oxidation to NO and HNO ₃	Pt–Rh
Acrylonitrile from propylene and ammonia	Bi–Mo, Fe–Sb (oxides)
Hydrogenation of vegetable oils	Ni
Sulfuric acid	V (oxide)
Oxidation of CO & hydrocarbons (car exhaust)	Pt, Pd
Reduction of NO _x (in exhaust)	Rh, vanadium oxide

Supported metal on SiO₂, have attracted substantial interest due to the importance of the silica–metal interface heterogeneous catalysis because the size and nature of the interaction of a metal particle with an oxide support are critical in

determining catalytic activity and selectivity. Silica-based materials are commonly used as heterogeneous catalysts (Table 2.1). A vast array of catalytically active materials could be come due to organic functionalization of amorphous, mesoporous, and zeolitic silica materials. In the perspective of catalysis, the term cooperativity refers to a system where at least two different catalytic entities act together to increase the rate of a reaction beyond the sum of the rates achievable from the individual entities alone.

After a reaction traditional heterogeneous catalysts can be recycled or could be used in a packed bed reactor, and the separation of the catalyst from the reaction mixture is simplified. Mesoporous silica is most common support for heterogeneous catalysts. Due to high surface area and low cost sometimes amorphous silica is also used, but pore structure and the irregularity of the surface can be detrimental in some applications. There is a large role of surface of silica support in the catalytic activity of heterogeneous catalysts. The weakly acidic silanol groups can form hydrogen bonds to reactants or transition states, leading to cooperative catalysis with surface organic groups. Silanols is weakly acidic and protic in nature, via hydrogen bonding thought to activate the electrophilic reactants, it expected that cooperative effect can be increases by introducing stronger acid groups onto the surface.

It is possible to prepare heterogeneous analogs of most, if not all, of the most commonly used soluble and homogeneous catalysts. Heterogenization through chemical surface modification is most conveniently carried out using a silica (or silica-rich) backbone.

CHAPTER 3:

LITERATURE REVIEW

CHAPTER 3

LITERATURE REVIEW

3.1 INTRODUCTION

Green chemistry, the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances, is an overarching approach that is applicable to all aspects of chemistry. From feedstocks to solvents, to synthesis and processing, green chemistry actively seeks ways to produce materials in a way that is more benign to human health and the environment. Catalysis is one of the fundamental pillars of green chemistry, the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances (Anastas et al., 2001). According to Corma et al. (1997) large number of solid acids in which the acidity can go from mild to the superacid level, acidity can be tuned and adapted to the particular reaction avoiding, to a large extent, other undesirable reactions to occur.

Many catalysts with highly desirable properties in terms of activity and selectivity have therefore not been commercialized for anything but the most valuable products. the catalyst is usually a dissolved metal complex. Furthermore, it is often possible to tune the chemoselectivity, regioselectivity, and/or

enantioselectivity of the catalyst (David et al., 2003). Wight et al. (2002) proposed that traditional heterogeneous catalysts are rather limited in the nature of their active sites and thus the scope of reactions that they can accomplish. Soluble organic catalysts can catalyze a much larger variety of reaction types than traditional solid catalysts but suffer from their inability (or high degree of difficulty) to be recycled.

Li et al. (2004) said immobilization of the chiral catalysts onto surfaces and into pores of solid inorganic supports such as microporous and mesoporous materials. The most important reactions surveyed for the chiral synthesis in porous materials include epoxidation, hydrogenation, hydroformylation, Aldol and Diels-Alder reactions, etc. The immobilisation of both inorganic and organic reagents onto a silica gel surface offers a number of advantages. When employed as catalysts, reactions are generally cleaner and exhibit improved selectivity towards the desired products compared to those of traditional homogeneous methods. The catalysts are easily separable from the reaction mixture and, in many instances, reusable (Price et al., 1999). The centers will be designed inspired not only on homogeneous Lewis acids, but also learning from the active centers of enzymes and biomolecules. Bioinspiration and molecular modeling will emerge as powerful strategies in catalyst design. These tools will be accompanied by new synthetic procedures in which the solids will be manipulated at the atomic level to assemble clusters that could act as active centers (Corma et al., 2002). Nanoscience and nanotechnology have become an ideal alternative for raising the industrial core competitiveness. It is also one of the areas where mankind expects

to realize the springing development. In fact nanocatalysis, a potent subfield emerged from nanoscience, has enormous potential to provide clean and safe alternatives to existing industrial practices that currently lack solutions (Sharma et al., 2013). A novel organic–inorganic hybrid heterogeneous catalyst was prepared through the immobilization of nickel tetrasulfophthalocyanine (NiTSPc) complex onto silica. The synthetic route is facile, cost effective and green. In addition, a novel chemical reactor with automated modes has been designed for the first time which opens up a new avenue for the effective and large scale degradation of dyes at room temperature using recyclable organic-inorganic hybrid catalyst (Sharma et al., 2012). ‘Green’ chemistry aims at the total elimination (or at least the minimization) of waste, and the implementation of sustainable processes. The utilization of nontoxic chemicals, renewable materials and solvent-free conditions are the key issues in a green synthetic strategy. The catalyst can also be recycled five times with only a moderate reduction in activity, making it acceptable for industrial-scale production (Wang et al., 2009). Alkynes are important skeleton in some natural products, pharmaceuticals, biologically active molecules, and nonlinear optical materials of the various approaches to synthesize symmetrical diynes and substituted alkynes, palladium-catalyzed homocoupling and Sonogashira crosscoupling of terminal alkynes are two of the most efficient routes (Wu et al., 2007)

3.1.1 PRINCIPLES OF GREEN CHEMISTRY

Developing green chemistry methodologies is a challenge that may be viewed through the framework of the “Twelve Principles of Green Chemistry”. These principles identify catalysis as one of the most important tools for implementing green chemistry (Anastas et al., 2001).

3.2 WORK DONE BY VARIOUS SCIENTIST

3.2.1 REVIEW ON GREEN CHEMISTRY

Chen et al. (2009) ‘Green’ chemistry aims at the total elimination (or at least the minimization) of waste, and the implementation of sustainable processes. The utilization of nontoxic chemicals, renewable materials and solvent-free conditions are the key issues in a green synthetic strategy. He works to develop new transformations that are not only efficient, selective, and high-yielding but that are also environmentally benign.

Corma et al. (2007) Worked on different methodology since beginning to be reached that the maximum strength of we have focused on the strength requirements of the the sites that can be obtained using mesoporous acid sites, their Bronsted or Lewis nature, and active aluminosilicates and zeolites in general does not allow location, to promote a particular transformation. the selection is generally believed that some other solids like sulhas been based on the idea of establishing a relation- fated zirconia or supported heteropolyacids are supership between the acid properties of the solids used as acids. It can, therefore, be expected that reactions catalysts and the outcome of reaction. Anastas et al.

(2001) Utilizing green chemistry for pollution prevention demonstrates the power and beauty of chemistry: through careful design, society can enjoy the products on which we depend while benefiting the environment. The economic benefits of green chemistry are central drivers in its advancement. Industry is adopting green chemistry methodologies because they improve the corporate bottom line. A wide array of operating costs is decreased through the use of green chemistry.

Sharma et al. (2012)-One of the challenging issues for chemists is to pursue green chemical transformations. Because of the huge amount of toxic wastes and by-products arising from chemical processes, chemists have been constrained to develop cost-effective and environmentally friendly catalytic routes that minimize waste. In this context, direct oxidative esterification of aldehydes with alcohols using environmentally benign oxidant, i.e. hydrogen peroxide in the presence of reusable heterogeneous catalyst under mild conditions is a facile, cost-effective, and environmentally friendly procedure that avoids the use of expensive activators and excess of reagents.

Hamilton et al. (2003)- The catalyst, solvent, or process may be very expensive, catalyst leaching may be too high, the solvent or ligand may be too expensive, or the pressure may be too high. Many approaches show considerable promise, but few detailed cost analyses have been carried out. They will be essential before any commercialization can be contemplated. An important property of some of the processes may be reduced environmental impact, as a result of recycling most of the components and getting away from volatile organic solvents with their polluting properties. Clark et al. (1999)- One of the major contributors to waste in

a chemical process is the separation of product/catalyst from the reaction mixture. This stage often generates large volumes of waste effluent (typically salts and contaminated aqueous streams) (Fig. 3.1). Also, the process of extracting the catalyst can often destroy the catalyst. Thus, elimination of this step would be favourable and is one of the major goals of green chemistry

Corma et al. (2002)- The development of new Lewis acid solids active and selective for catalytic oxidations is an urgent need and a challenging scientific target for some substrates especially using environmentally friendly oxidants. Since the replacement of current stoichiometric oxidations for the production of fine chemicals by environmentally benign catalytic oxidations is one of the major tasks in green chemistry, solid Lewis acids are called to play a crucial role to accomplish this goal.

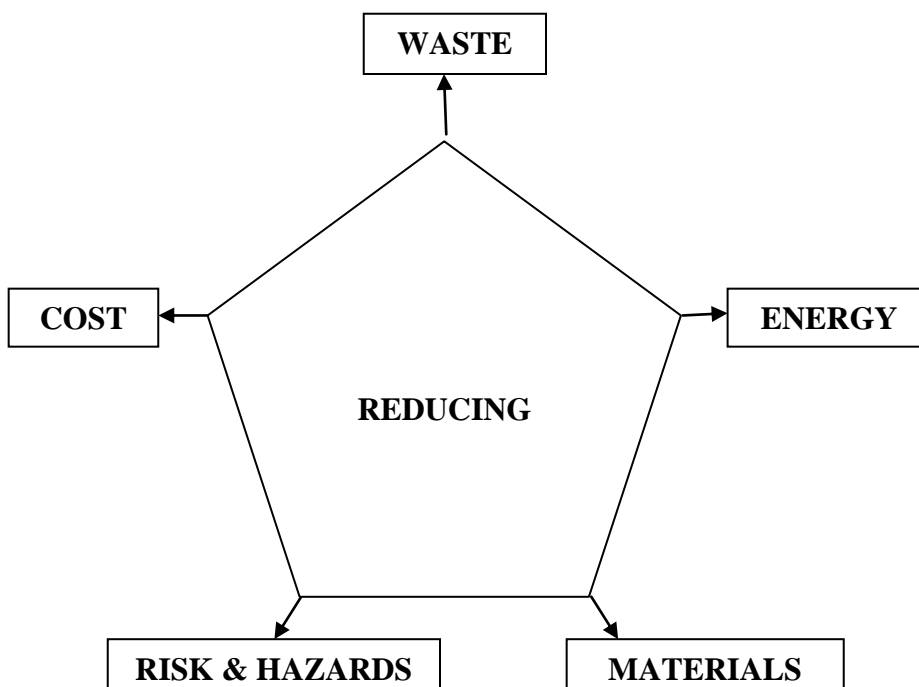


Fig. 3.1: Green Chemistry (elements).

3.2.2 REVIEW ON CATALYST

Najera et al. (2003)- Phosphane-free oxime-derived palladacycle 8a, is an efficient and versatile pre-catalyst for the amine- and copper-free Sonogashira-type reaction of aryl iodides and aryl- and vinyl bromides with a variety of terminal acetylenes. The catalytic system has also been successfully applied to the cross-coupling of aryl iodides with alkynylsilanes. Metal-catalyzed acetylenic homo- and cross-coupling processes are currently under intensive study due to the presence of the alkynyl moieties in a wide range of natural and unnatural organic materials.

Sharma. et al. (2008)- Gallic acid was immobilized on Amberlite XAD-16 by coupling it through –N N group. The resulting chelating resin AmberliteXAD-16 gallic acid, characterized by thermogravimetric analysis (TGA), infrared (IR) spectra and BET analysis, was used to preconcentrate Cr(III), Mn(II),Fe(III),Co(II), Ni(II) and Cu(II)ions. Major sources of heavy metals in the environment includemetal extraction,metal refining, electroplating, paints and pigments, the manufacture of batteries as well as metal discharges from industrial facilities. So, there is a critical need for preconcentration and separation of the of trace metals from matrices prior to their determination, due to their frequent presence in environmental samples and higher matrix interferences.

Marder et al. (2004)- Palladium-catalyzed terminal alkyne dimerization, through oxidative homocoupling, is a useful approach to the synthesis of symmetrical 1,4-diynes. This reaction might be accomplished in the absence of intentionally added stoichiometric oxidants (to reoxidize Pd(0) to Pd(II)). The presence of a

stoichiometric quantity of air (or added oxidant such as I₂) is essential for alkyne dimerization.

Sharma et al. (2012)- a novel organic–inorganic hybrid heterogeneous catalyst was prepared through the immobilization of nickel tetrasulfophthalocyanine (NiTSPc) complex onto silica. The synthetic route is facile, cost effective and green. The hybrid catalyst showed up to 96% of degradation efficiency, and can be recovered and reused for multiple cycles without appreciable loss in its catalytic activity. In addition, a novel chemical reactor with automated modes has been designed for the first time which opens up a new avenue for the effective and large scale degradation of dyes at room temperature using recyclable organic inorganic hybrid catalyst.

Tsai et al. (2007)- A cationic 2,2'-bipyridyl palladium(II)/CuI system was proven to be a reusable and highly efficient catalyst for the homocoupling of terminal alkynes at room temperature using water as a solvent in the presence of TBAB under aerobic conditions. The water-soluble catalytic system was separated from the organic products by extraction and the residual aqueous solution showed activity for reuse for several cycles without a significant decrease in activity.

Sajiki et al. (2007)- A facile and environmentally friendly synthetic method for a variety of symmetrical 1,3-diyne derivatives based on the Pd/C–CuI-catalyzed homocoupling reaction of terminal alkynes has been developed. 1,3-Diynes are of significant importance as building blocks or synthetic intermediates for numerous bioactive natural products-1 and pharmaceuticals-2 including antifungal agents.

Wu et al. (2007)- Alkynes are important skeleton in some natural products,

pharmaceuticals, biologically active molecules, and nonlinear optical materials. the various approaches to synthesize symmetrical diynes and substituted alkynes, palladium-catalyzed homocoupling and Sonogashira cross-coupling of terminal alkynes are two of the most efficient routes. For the successful palladium-catalyzed homocoupling of terminal alkynes, an oxidant is necessary besides phosphine ligands, CuI and the additive such as TBAB as described in detail by Fairlamb and co-workers.

Li et al. (2005)- An efficient method for palladium-catalyzed homocoupling reaction of terminal alkynes in the synthesis of symmetric diynes is presented. The results showed that both Pd(OAc)₂ and CuI played crucial roles in the reaction. In the presence of 2 mol % Pd(OAc)₂, 2 mol % CuI, 3 equiv of Dabco, and air, homocoupling of various terminal alkynes afforded the corresponding symmetrical diynes in moderate to excellent yields, whereas low yields were obtained without either Pd(OAc)₂ or CuI.

Stolle et al. (2011)- A method for the Glaser coupling reaction of alkynes by using a vibration ball mill has been developed. The procedure avoids the use of ligands and solvents during the reaction. Aryl- and alkyl-substituted terminal alkynes undergo homocoupling if coground with KF–Al₂O₃ and CuI as a milling auxiliary and catalyst.

Sharma et al.(2012)- The resin was found to be highly selective for Pd(II) ions in the pH range 4–5 with a very high sorption capacity of 0.73 mmol/g and preconcentration factor of 335. Palladium and its alloys have an extensive range of applications in various fields such as dentistry, metallurgy, instrument

manufacturing, and chemical industries. The most significant and prevalent application of palladium is in the field of catalysis and automotive catalytic converters which leads to its accumulation in the environment.

Beifuss et al. (2009)-The efficient Cu(I)-catalyzed oxidative homocoupling of terminal alkynes in the presence of a base using an amine as a ligand and oxygen as an oxidant yields the symmetrical 1,3-diynes with yields of up to 99%. The outcome of the couplings critically depends on the proper choice of base and ligand as well as reaction conditions. Best results were observed with 2.0 mol% CuCl, 1.5 mol% TMEDA or DBEDA, and DBU or DABCO in acetonitrile.

The further development of the Cu(I) salt catalyzed coupling using O₂ as an oxidant appeared to be the most attractive approach in order to meet the demand for high yields and high selectivities, simple experimental procedures under mild reaction conditions, avoidance of expensive and/or harmful reagents, and use of O₂ as an environmentally benign oxidant.

Chen et al. (2009)- Describe a green approach towards the synthesis of conjugate 1,3-diyne. Conjugate 1,3-diyne derivatives are very important materials in the fields of biology and materials science, because they can be converted into various structural entities, especially substituted heterocyclic compounds. The catalyst can also be recycled five times with only a moderate reduction in activity, making it acceptable for industrial-scale production

Sharma et al. (2013)-fabrication of a novel and highly efficient silica nanospheres-based palladium catalyst (SiO₂@APTES@Pd-FFR) via immobilization of a palladium complex onto silica nanospheres functionalized

with 3-aminopropyltriethoxysilane (APTES), and its catalytic application for the oxidative amination of aldehydes to yield commercially important amides. The nano-catalyst was found to be highly effective for the oxidative amination of aldehydes using hydrogen peroxide as an environmentally benign oxidant to give amides.

Mizuno et al. (2009)-An easily prepared supported copper hydroxide on titanium oxide ($\text{Cu}(\text{OH})_x/\text{TiO}_2$) showed high catalytic performance for the 1,3-dipolar cycloaddition of organic azides to terminal alkynes in non-polar solvents under anaerobic conditions. The reactions of various combinations of organic azides (four examples, including aromatic and aliphatic ones) and terminal alkynes (eleven examples, including aromatic, aliphatic, and double bond-containing ones) exclusively proceeded to give the corresponding 1,4-disubstituted-1,2,3-triazole derivatives in a completely regioselective manner.

Sharma et al. (2014)- Efficient, selective and reusable acetoacetanilide-functionalized Fe_3O_4 nanoparticles were developed for the first time for the removal of Pb^{2+} ions. A comprehensive characterization of the functionalized nanoparticles, at different levels of synthesis, was carried out by TEM, EDS, XRD, SEM, FT-IR and VSM. The adsorption equilibrium obeyed the Langmuir isotherm model with a maximum enrichment capacity of 392.2 mg/g at 318 K. A superparamagnetic core provided ease of separation, while silica shell encapsulation endowed superior dispersibility and stability to the nanoparticles, by preventing their aggregation and chemical decomposition.

Sharma et al. (2012)- The ester functionality is present ubiquitously in the structure of significant natural and synthetic molecules; therefore, constitutes an important synthetic target in the pharmaceutical industry, materials science, organic and bioorganic synthesis, etc. Esterification is traditionally a two-step procedure that involves the activation of the carboxylic acid as an acyl halide, anhydride, or activated ester followed by nucleophilic substitution. An attractive alternative is the direct catalytic transformation of alcohols or aldehydes to esters under mild conditions, without the use of the corresponding acid or acid derivative.

3.3 GRAFTING METHOD FOR CATALYST (CO-VALENT GRAFTING)

Wight A. et al. (2002)-Chlorination of the silica surface followed by subsequent reaction with Grignard reagents can be used to form silicon-carbon bonds (Fig. 3.2).

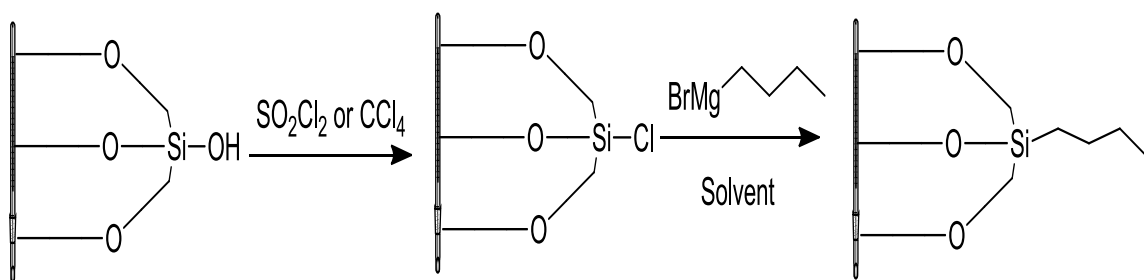


Fig. 3.2: Chlorination and Subsequent Reaction with a Grignard Reagent to Functionalize Silica.

The use of Grignard reagents limits the variety of functional groups that can be tethered to the surface. However, the formation of a silicon-carbon bond between

the organic moiety and the surface is desirable because of the stability of the Si-C bond. Another well-studied technique of silica surface functionalization is the grafting of organic groups onto a silanol-containing surface using a trichloroor trialkoxy- organosilane (Fig. 3.3).

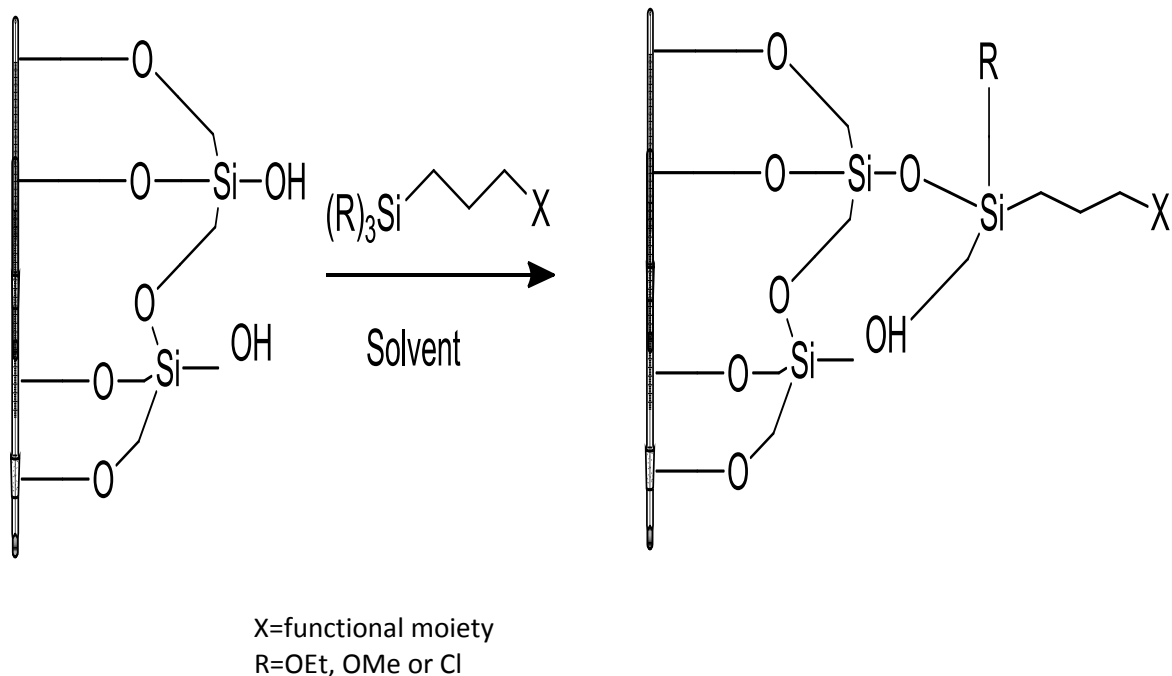


Fig. 3.3: Example of Grafting Organosilanes onto a Silanol-Containing Surface.

Numerous organosilanes are commercially available. Additionally, techniques for synthesizing organosilanes are documented in the literature (e.g. Fig 3.4). The availability of the silanol groups can determine whether the grafted silicon atom is tethered via one, two, or three silicon-oxygen bonds.

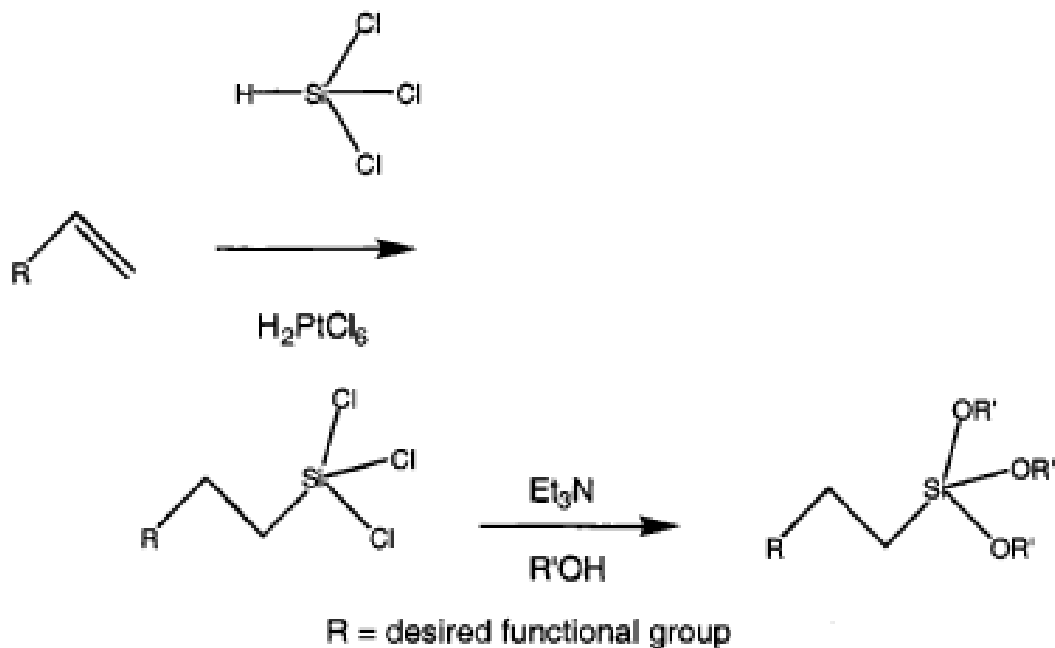


Fig. 3.4: Synthetic Route to Organosilanes.

These types of silicon atoms are denoted as T1 ($\text{MeSi}(\text{OSi})(\text{OR}\phi)_2$), T2 ($\text{MeSi}(\text{OSi})_2(\text{OR}\phi)$), and T3 ($\text{MeSi}(\text{OSi})_3$) sites, respectively. The R functionality can be either an alkyl or H (if water is present to cause the hydrolysis). In the absence of water, the chloro-organosilanes require an amine, e.g., triethylamine, for the reaction with surface silanols to proceed. This is not the case with alkoxy-organosilanes (Fig. 3.5).

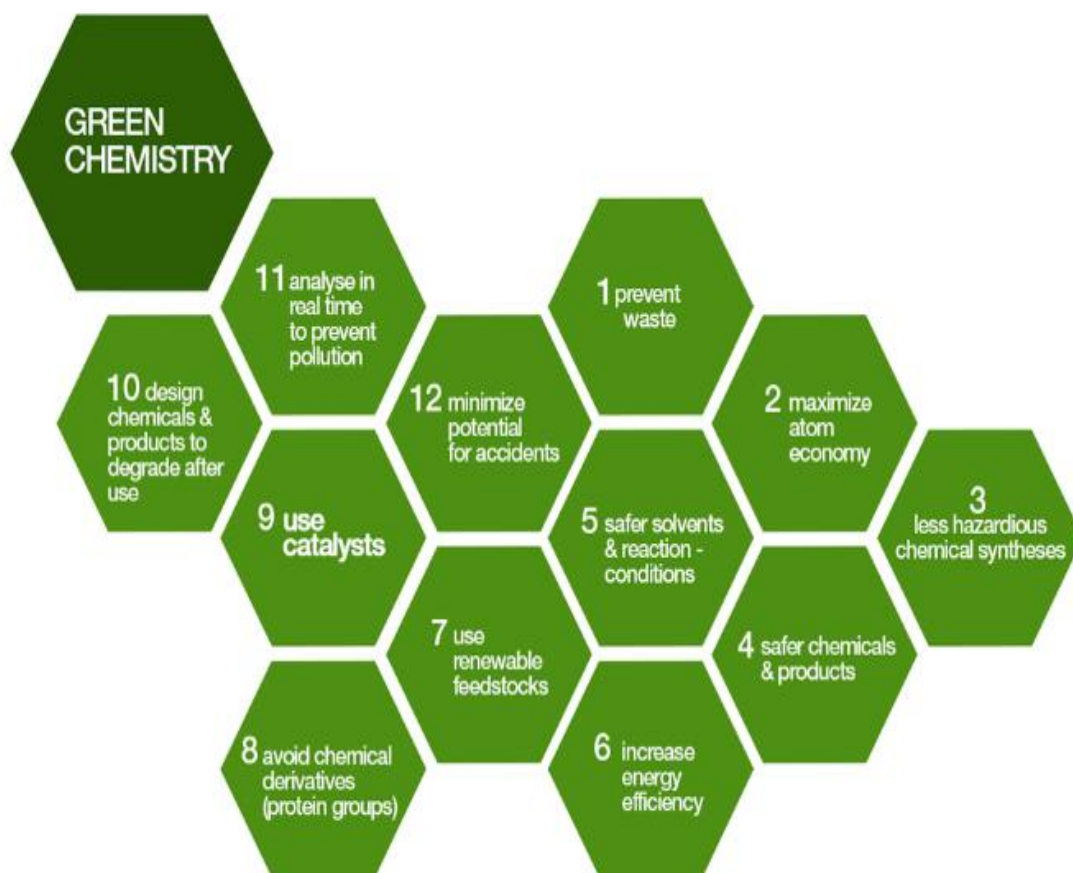


Fig. 3.5: Green chemistry overview.

CHAPTER 4:

EXPERIMENTAL

CHAPTER 4

EXPERIMENTAL

4.1 MATERIALS AND REAGENTS

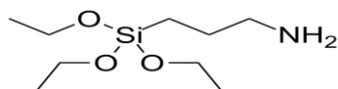
3-Aminopropyltriethoxysilane (APTES) (Fluka), silica gel (Qualigens), salicylaldehyde (Sisco Pvt. Ltd, India), Copper acetate (Thomas Baker) were commercially obtained and used as received without further purification. All other starting materials and reagents used in the reactions were obtained from Spectrochem and Alfa Aesar.

4.1.1 CHEMICAL DESCRIPTION

Chemical name- 1-Propanamine, 3-(triethoxysilyl)

Molecular formula- $C_9H_{23}NO_3Si$

Structural formula-



Molecular Weight- 221

Purity- 98% to 100%

Melting point -70° C

Boiling point- 223° C

Density -0.946g/ml at 25°C(lit)

It is an aminosilane frequently used in the process of silanization, the functionalization of surfaces with alkoxy silane molecules. Application- Forms aminopropyl derivative of glass, an adsorbent for affinity chromatography. Used to prepare positively charged slides suitable for use with various immunohistochemical and in situ hybridization procedures. Recently (3-Aminopropyl)triethoxysilane has been used to prepare dye-doped silica nanoparticles with minimal aggregation and minimal nonspecific binding with biomolecules.

Chemical Name- Silica Gel

Molecular formula- SiO_2

Molar mass- 60.08 g/mol

Appearance- transparent beads

Odor- Odorless

Silica is one of the most complex and most abundant families of materials, existing both as several minerals and being produced synthetically. Under exposure to oxygen, a silicon surface oxidizes to form silicon dioxide (SiO_2). Thermal oxidation of silicon is easily achieved by heating the substrate to temperatures typically in the range of 900-1200 degrees C.

Silica gel's high specific surface area (around $800 \text{ m}^2/\text{g}$) allows it to adsorb water readily, making it useful as a desiccant (drying agent). Silica gel is often described as "absorbing" moisture, which may be appropriate when the gel's

microscopic structure is ignored, as in silica gel packs or other products. However chemically, material silica gel removes moisture by *adsorption* onto the surface of its numerous pores rather than by *absorption* into the bulk of the gel.

Chemical name- salicylaldehyde

Molecular Formula: C₇H₆O₂

Density: 1.15 g/cm³

Molar mass: 122.12 g/mol

Boiling point- 197°C(lit.)

Along with 3-hydroxybenzaldehyde and 4-hydroxy benzaldehyde, it is one of the three isomers of hydroxy benzaldehyde. This colorless oily liquid has a bitter almond odor at higher concentration. Salicylaldehyde is a key precursor to a variety chelating agents, some of which are commercially important.

4.2 PHYSICOCHEMICAL CHARACTERIZATIONS

The IR spectra were recorded on Perkin Elmer Spectrum 2000 FT-IR spectrometer. Powder X-ray diffraction (XRD) patterns of the samples were obtained on a Bruker D8 ADVANCE X-ray diffractometer. Scanning electron microscopy (SEM) images were obtained using a ZEISS EVO 40 instrument. Elemental analysis (CHN) was done using an Elementar Analysensysteme GmbH VarioEL V3.00. Solid-state ¹³C (CPMAS) NMR spectra were recorded on a Bruker DSX-300 NMR spectrometer. The BET surface areas were obtained using a Gemini- V2.00 instrument (Micromeritics Instrument Corp.) and for that solid samples were outgassed under vacuum in order to eliminate physisorbed

moisture. Energy dispersive X-ray fluorescence spectroscopy was performed on Fischer scope X-Ray XAN-FAD BC. The homocoupling products obtained were analyzed and confirmed on Agilent gas chromatography (6850 GC).

Silica-based materials are commonly used as heterogeneous catalysts. Organic functionalization of amorphous, mesoporous, and zeolitic silica materials leads to a vast array of catalytically active materials. In the context of catalysis, the term cooperativity refers to a system where at least two different catalytic entities act together to increase the rate of a reaction beyond the sum of the rates achievable from the individual entities alone.

Traditional heterogeneous catalysts can be recycled after a reaction or used continuously in a packed bed reactor, and the separation of the catalyst from the reaction mixture is simplified. One of the most common supports for heterogeneous catalysts is mesoporous silica. Amorphous silica is sometimes used due to its high surface area and low cost, but the irregularity of the surface and pore structure can be detrimental in some applications.

Co-valent grafting

In this technique, the solid support is synthesized first, and the surface is subsequently modified with chemical functional groups. Using this method the catalyst may be immobilized in one step or in a step-by-step fashion as commonly utilized in solid phase synthesis. This method has been investigated extensively due to the variety of chemistries that can be performed. Since the catalyst and support are synthesized in different steps, the catalyst choice is not limited by the reaction conditions of the solid support synthesis. In addition, the solid support

and small molecule modifiers can be thoroughly characterized prior to immobilization. This becomes important because characterization of the completed solid supported catalysts can be hindered by low catalyst loadings.

4.3 CATALYST PREPARATION

First of all, silica gel was functionalized with 3-aminopropyltriethoxysilane to give amine functionalized silica gel ($\text{SiO}_2\text{@APTES}$) according to the reported procedure. Then, $\text{SiO}_2\text{@APTES}$ and salicylaldehyde were dispersed in the ethanol and refluxed for 18 h to afford silica based schiff base ligand ($\text{SiO}_2\text{@APTES@SAL}$). Finally the copper acetate was added in half molar ratio (Fig. 4.1) and mixture was stirred for 3 hours. The solvents were evaporated and the product was dried overnight in vacuum to give catalyst ($\text{SiO}_2\text{@APTES@SAL-Cu}$)

By incorporating the above mentioned methodology, various organic –inorganic silica based catalyst have been designed for industrially significant organic transformation.

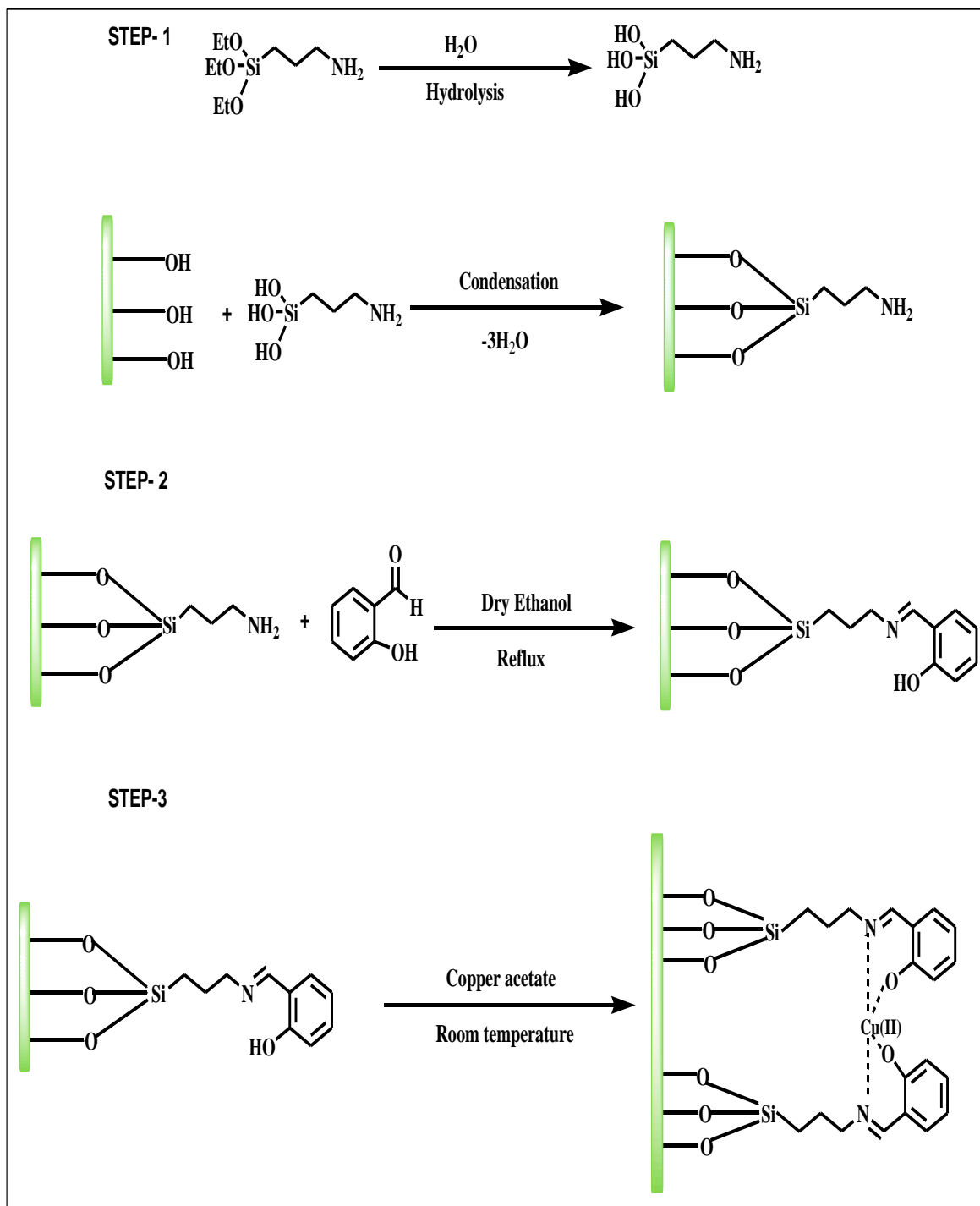


Fig 4.1: Preparation of silica based organic-inorganic hybrid copper catalyst ($\text{SiO}_2\text{@APTES@SAL-Cu}$).

The surface of the silica support can itself play a large role in the catalytic activity of heterogeneous catalysts. The weakly acidic silanol groups can form hydrogen bonds to reactants or transition states, leading to cooperative catalysis with surface organic groups. Because the protic nature of the weakly-acidic silanols is thought to activate the electrophilic reactants via hydrogen bonding, it follows that introducing stronger acid groups onto the surface could be expected to increase the cooperative effect.

It is possible to prepare heterogeneous analogs of most, if not all, of the most commonly used soluble and homogeneous catalysts. Heterogenization through chemical surface modification is most conveniently carried out using a silica (or silica-rich) backbone.

4.4 GENERAL EXPERIMENTAL PROCEDURE FOR HOMOCOUPLING REACTION

A mixture of terminal alkyne (1 mmol), NaOAc (1 mmol) acetonitrile (2 mL) and SiO₂@APTES@SAL-Cu catalyst (20 mg) was refluxed at room temperature. Upon completion of reaction, the catalyst was recovered by filtration. The aqueous solution was then extracted with ethylacetate. Further, the organic phase was dried over sodium sulphate and the solvent was removed under vacuum. Finally, the diene products were analyzed and confirmed by GC-MS.

CHAPTER 5:

RESULTS AND DISCUSSIONS

CHAPTER 5

RESULTS AND DISCUSSIONS

5.1 CATALYST CHARACTERIZATIONS

5.1.1 FTIR SPECTRA ANALYSIS

The silica-based materials SiO_2 , $\text{SiO}_2\text{@APTES}$ and $\text{SiO}_2\text{@APTES@SAL-Cu}$ were characterized by FT-IR spectroscopy and the results are presented in Fig. 5.1. The spectrum of silica gel shows a peak at 948 cm^{-1} corresponds to stretching vibrations of Si-OH. However, on moving from SiO_2 to $\text{SiO}_2\text{@APTES}$, there is a significant decrease in the intensity of Si-OH stretching vibration bands because of reaction between the surface silanol groups of SiO_2 and ethoxy groups of APTES during surface modification. Apart from this, two new peaks in the range of $2900\text{--}2800\text{ cm}^{-1}$ are observed due to CH_2 groups of linking agent which confirmed that APTES has been attached to silica gel. Further, the spectrum of the $\text{SiO}_2\text{@APTES@SAL-Cu}$ shows a strong band at 1648 cm^{-1} due to C=N stretching vibration resulting from Schiff condensation between the NH_2 group and carbonyl group of ligand. The spectrum of recovered catalyst and fresh catalyst are also compared. It can be observed that there is not much difference between the two spectra.

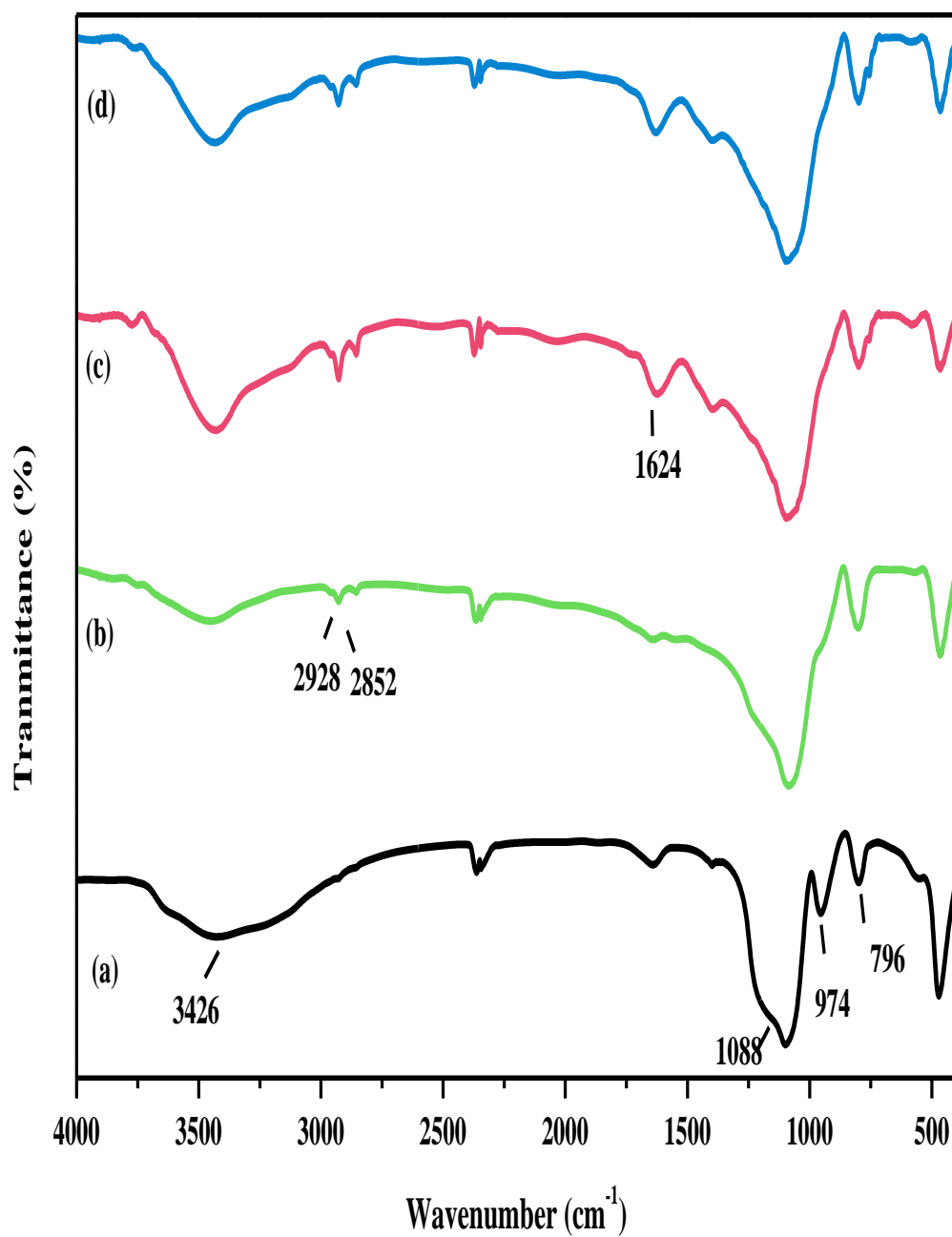


Fig. 5.1: FT-IR spectra of (a) SiO₂, (b) SiO₂@APTES and (c) SiO₂@APTES@SAL-Cu (d) recovered SiO₂@APTES@SAL-Cu

5.1.2 XRD ANALYSIS

X-ray diffraction (XRD) analysis was carried out in order to investigate the structure of SiO_2 , $\text{SiO}_2\text{@APTES}$ and $\text{SiO}_2\text{@APTES@SAL-Cu}$ and the results are presented in Fig. 5.2. The broad peak centred around $2\Theta = 23^\circ$ in the all the three XRD patterns is ascribed to the diffraction peak of amorphous silica, which clearly depicts that there is no change in the topological structure of SiO_2 before and after surface functionalization reactions.

However, there is a slight decrease in intensity observed after successive immobilization of APTES and copper complex. The decreasing trend in the XRD peaks intensity can be attributed to the lowering of local order, such as variation in wall thickness, which might be due to the reduction of scattering contrast between the walls of the silicate framework and the covalently anchored SAL-Cu in the pores.

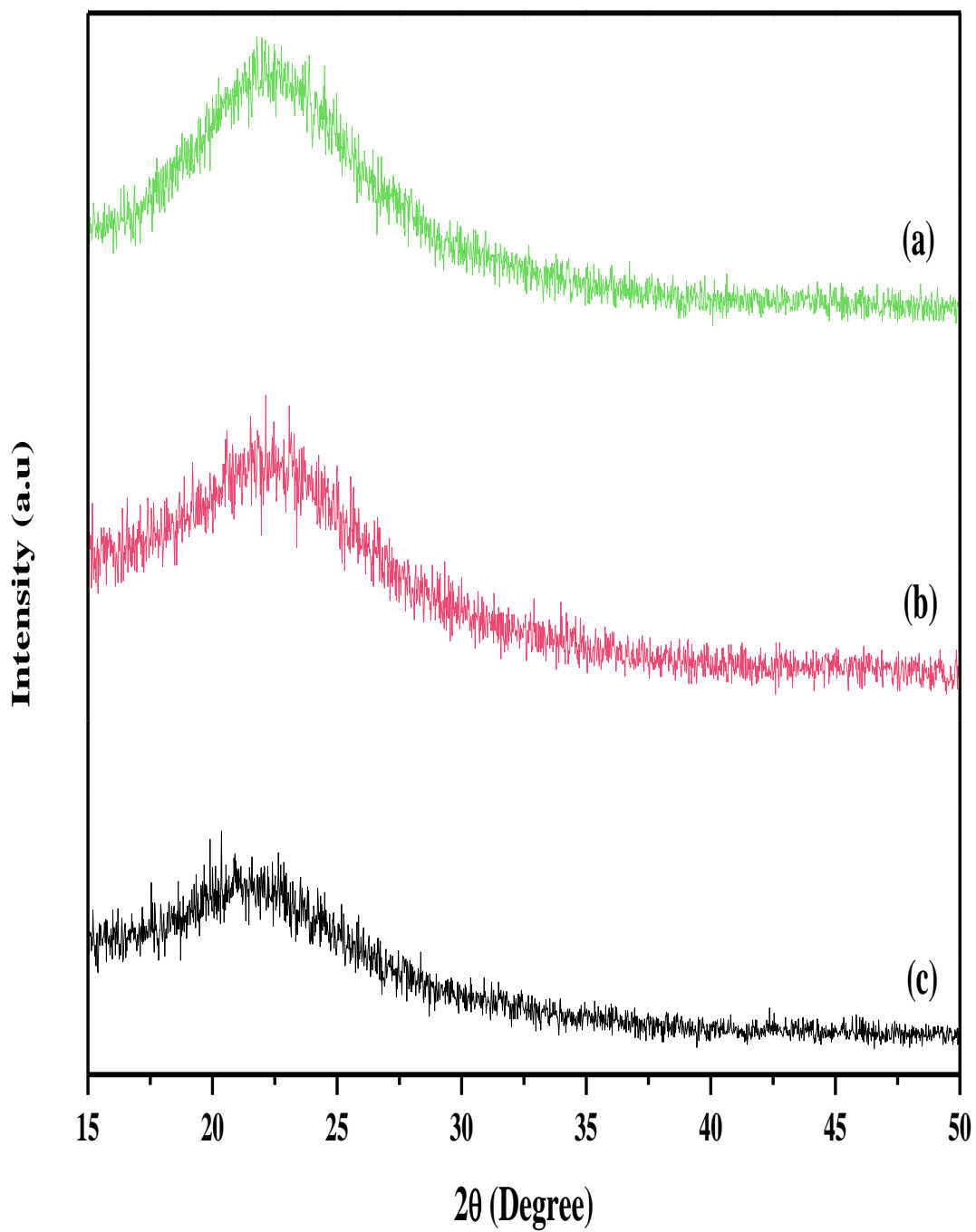


Fig. 5.2: XRD diffraction patterns of (a) SiO_2 , (b) $\text{SiO}_2\text{@APTES}$ and (c) $\text{SiO}_2\text{@APTES@SAL-Cu}$ 3.1.3 SEM analysis

The morphology of the catalyst is characterized by scanning electron microscopy. SEM images of silica gel and catalyst are shown (Fig. 5.3). It can also be seen that the physical surface of silica gel after immobilisation remains unchanged from the original morphology. Moreover, silica gel beads do not possess any cracks during the preparation of catalyst confirming its good mechanical strength. It can be also be inferred that there is a uniform dispersion of copper acetate and salicylaldehyde on the surface of silica which is responsible for its high activity.

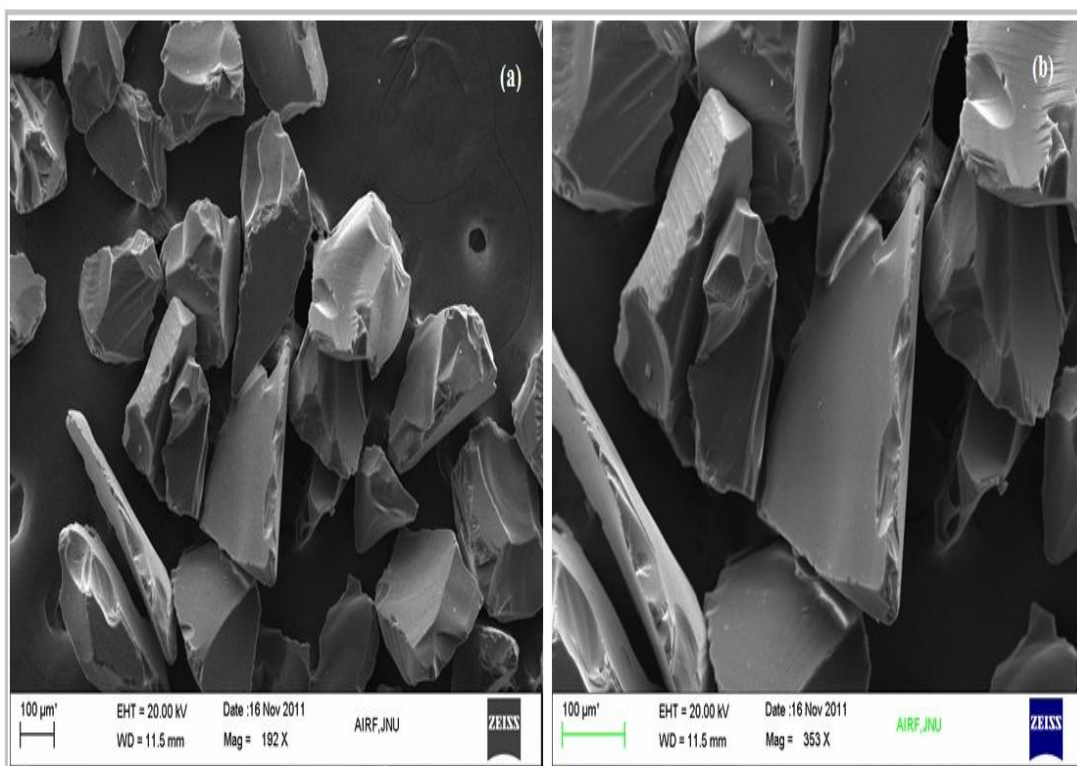


Fig. 5.3: SEM images of (a) silica gel (b) SiO₂@APTES@SAL-Cu catalyst

5.1.3. SOLID STATE ^{13}C CPMAS NMR SPECTROSCOPY

The functionalization of SiO_2 with APTES linking agent was confirmed by solid state ^{13}C CPMAS NMR spectroscopy. The ^{13}C NMR spectrum of $\text{SiO}_2@\text{APTES}$ shows the presence of three well resolved peaks at $\delta = 9.3, 22.3$ and 42.9 ppm which can be assigned to due to $-\text{Si}-\text{CH}_2-$, $-\text{CH}_2-$ and $-\text{N}-\text{CH}_2-$ groups of APTES onto the surface of silica gel (Fig. 5.4a) . This validates the covalent immobilization of APTES onto the surface of SiO_2 . Fig. 5.4b shows ^{13}C NMR spectrum spectrum of $\text{SiO}_2@\text{APTES}@\text{SAL}$.

Upon immobilization of salicylaldehyde to aminefunctionalized silica gel, there is a shift of $-\text{N}-\text{CH}_2-$ peak to 63.29 ppm. The peak at 41.5 ppm refers to the uncomplexed $-\text{N}-\text{CH}_2-$ group. The peaks correspond to ring carbon atoms are expected to appear in the aromatic region. However, the resolution of these peaks in solid state NMR was not achieved under the analysis conditions and therefore, the spectrum showed four broad peaks. Further, $-\text{C}=\text{N}$ peak at 161.4 ppm confirms Schiff base condensation between aminopropyl silica gel and salicylaldehyde ligand.

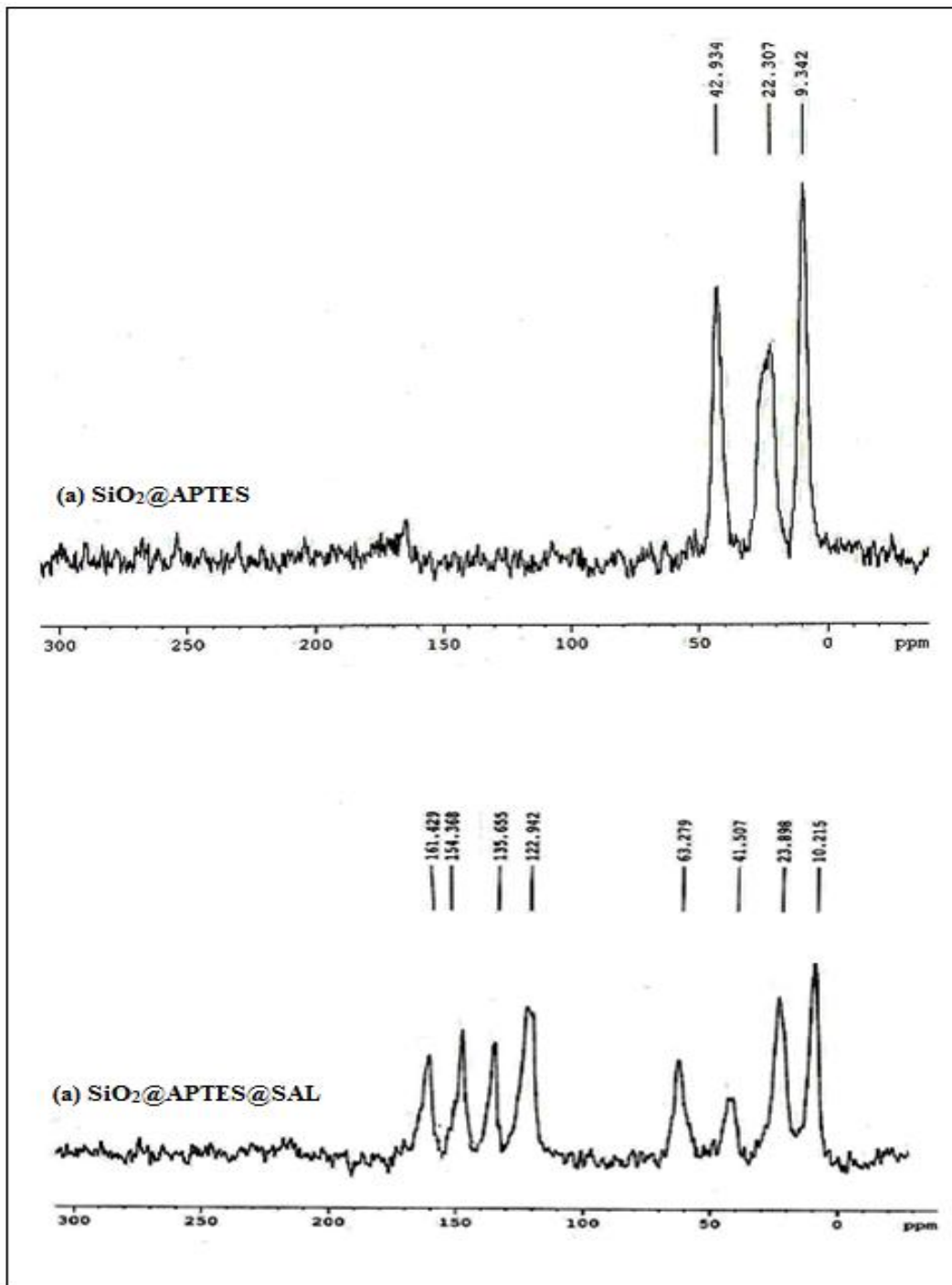


Fig. 5.4: ^{13}C CPMAS NMR spectrum of (a) $APTES@SiO_2$ and (b) $SiO_2@APTES@SAL$.

5.1.4 ELEMENTAL AND BET SURFACE AREA ANALYSIS

The specific surface areas of the synthesized silica based samples have been calculated using the Brunauer-Emmett-Teller (BET) method and the results have been presented in the Table 5.1. As expected, the surface area of SiO₂ gets reduced from 232.45 to 155.11 m²g⁻¹ after functionalization of the APTES and it was further reduced to 129.53 m²g⁻¹ upon anchoring the 2-hydroxyacetophenone copper complex. The reduction in the surface area is due to the immobilization of organic moieties onto the porous silica matrix which eventually blocks the access of nitrogen gas molecules.

This observation directly confirms the successive anchoring of APTES and copper complex onto the surface of SiO₂. Table 5.1 also lists the chemical compositions of all the synthesized silica based materials. It is seen that reasonable amount of increment in the content of both carbon and nitrogen were detected on moving from SiO₂ to SiO₂@APTES. Further, the elemental analysis data of SiO₂@APTES shows that carbon and nitrogen contents are 5.17 % and 1.26% respectively.

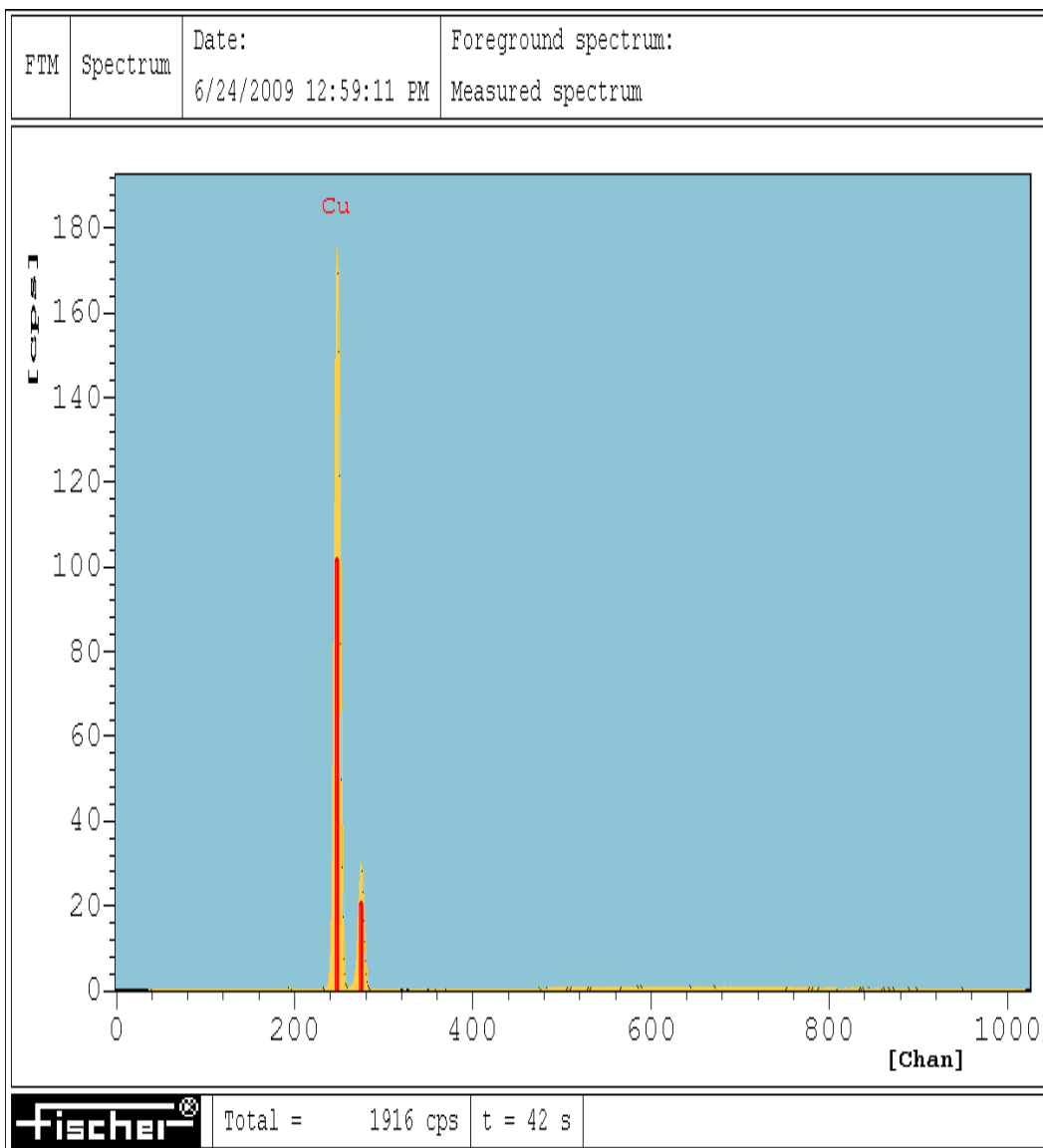
Based on these results the C/N ratio has been calculated to be ~2.9 which is close to the theoretical value thereby confirming the incorporation of APTES linking agent into the silica matrix. Apart from this, the well resolved peak of copper in the ED-XRF spectrum of SiO₂@APTES@2HAP-Cu (Fig. 5.5) also provides the clear evidence of the immobilization of copper complex on the modified silica gel.

The newly designed catalyst works under mild reaction conditions and also exhibits excellent performance in terms of good product yield and high turnover number (TON).

One of the most important attributes of the present methodology is that the catalyst can be recycled several times without any appreciable loss in its activity as proved by FTIR Spectroscopy and SEM analysis. Besides, the heterogeneity test also confirms that no leaching of active catalytic species occurs from the silica supported zinc catalyst which confirms its remarkable structural stability under the applied reaction conditions.

Table 5.1: Physico-chemical parameters of SiO₂, SiO₂@APTES and SiO₂@APTES@SAL-Cu

Nano-material	Elemental Analysis			BET surface area (m ² g ⁻¹)
	C(%)	H(%)	N(%)	
SiO ₂	-	-	-	232.45
SiO ₂ @APTES	5.17	1.26	1.81	155.11
SiO ₂ @APTES@SAL-Cu	12.88	2.15	3.35	129.53



Meas. para. (foreground spectrum):

High voltage = 50 kV (875) Prim. Filter = Al1000

Collimator 4 = 2.00 Dm. Anode current 138 uA

Meas. distance = 0.04 mm

List of spectra:

Foreground: Measured spectrum

Fig. 5.5: ED-XRF spectrum of SiO₂@APTES@2HAP-Cu catalyst.

5.2 CATALYTIC ACTIVITY TEST

5.2.1 Catalytic Performance

Catalytic performance of silica supported organic-inorganic hybrid zinc complex was evaluated in the one pot synthesis of 1, 4 disubstituted triazoles derivatives using phenyl acetylene and benzyl bromide as test substrates. In order to obtain an optimum reaction profile for SiO₂@APTES@2HAP-Cu mediated triazoles synthesis, the effect of different reaction parameters such as amount of catalyst, reaction time and temperature, substrate molar ratio and type of solvent have been studied in detail.

5.2.2 Effect of Amount of Catalyst

In order to examine the effect of amount of catalyst on oxidative homocoupling of terminal alkynes, phenylacetylene was chosen as test substrate and results are presented in (Fig. 5.6). It can be seen that the oxidative homocoupling of phenylacetylene did not proceed in the absence of catalyst. The conversion of phenylacetylene increased with increase in the amount of SiO₂@APTES@SAL-Cu catalyst up to 25 mg. However, when 25 mg of the catalyst was used, maximum conversion of phenylacetylene was obtained. Further increase in the amount of catalyst did not produce any significant increase in the conversion percentage. Hence, SiO₂@APTES@SAL-Cu is a highly efficient heterogenized solid catalyst for the homocoupling of phenyl acetylene into 1,4-diphenylbuta-1,3-diyne.

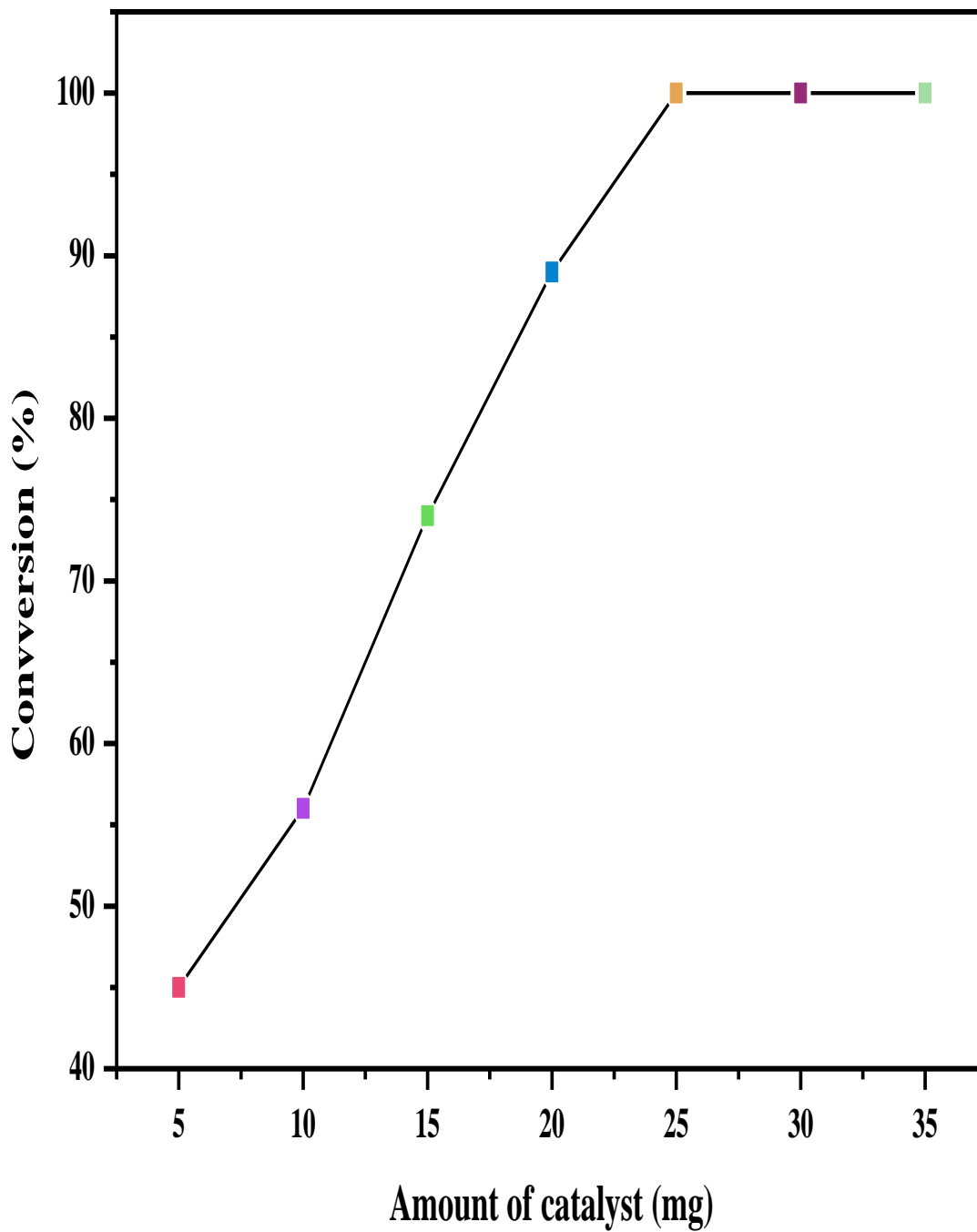


Fig. 5.6: Effect of amount of catalyst the model reaction (Reaction conditions: phenylacetylene (1 mmol), NaOAc (1 mmol) acetonitrile (2 mL) and SiO₂@APTES@SAL-Cu catalyst, room temperature, 3 h).

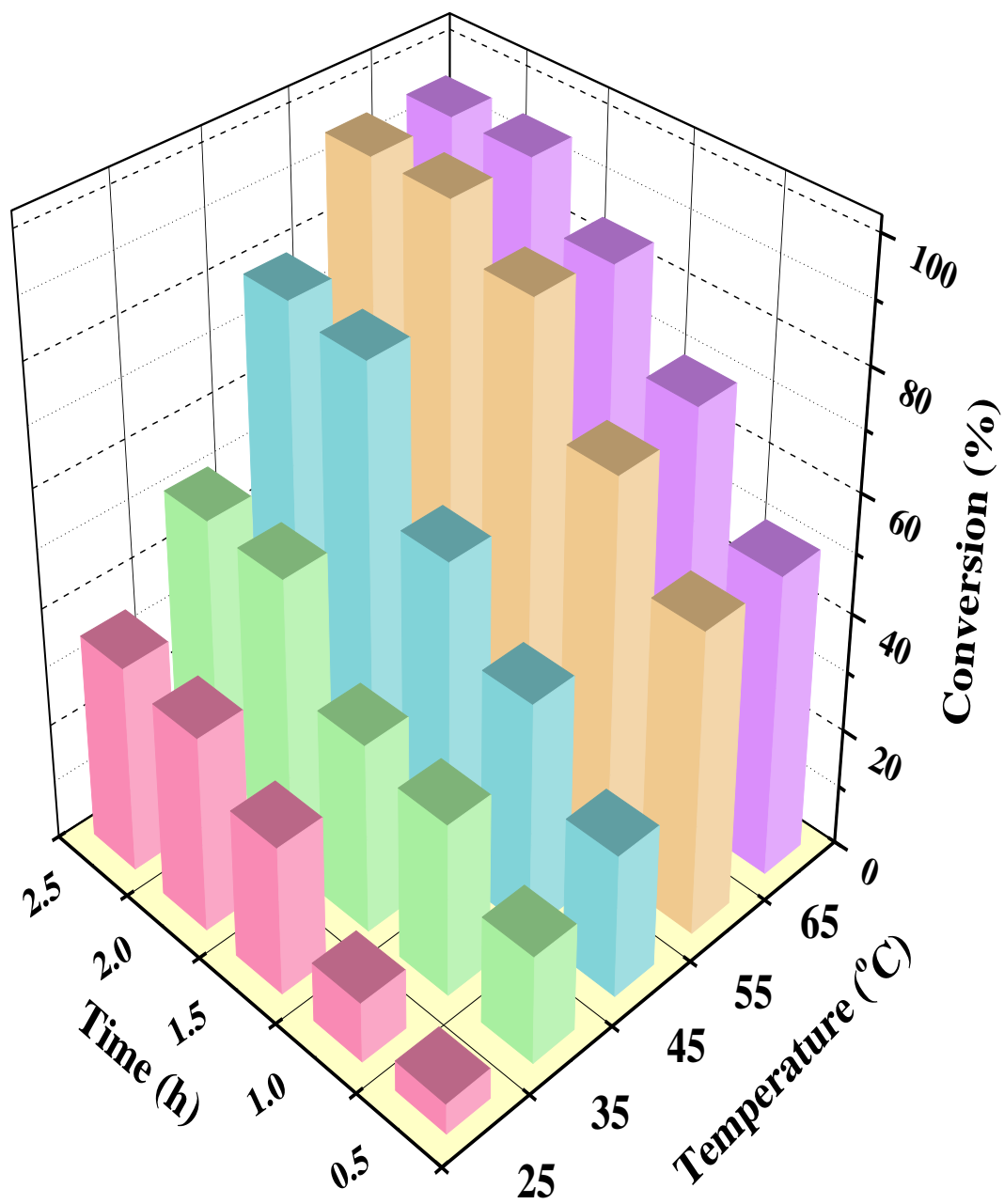


Fig 5.7: effect of time and temperature on reaction

5.2.3 Effect of Time and Temperature

In order to examine the effect of time and temperature, the model reaction was performed under a diverse range of temperatures (25-65°C) for different time

periods (0.5-2.5 h) and the results have been summarized in Figure 5.7. The reaction time had a remarkable influence on the one pot synthesis of triazoles. Detailed examination of the results revealed that a time period of 2 h was appropriate for the maximum conversion of the reactants when the reaction was carried out at 55 °C.

5.2.4 Effect of Substrate Molar Ratio

Having established 1: 1 mixture of water/^tBuOH as the best solvent for the click reaction, we then investigated the influence of substrate ratio and the results are summarized in Figure 5.8. Different molar ratios of phenyl acetylene, benzyl bromide and sodium azide (1:0.5:0.5, 1:1:1, and 1:2:2) were considered while keeping the other parameters fixed. Upon utilizing 1:0.5:0.5 substrate ratio, moderate conversion was observed. When equal molar ratio of all the three substrates was applied, the reaction time was shortened and maximum conversion was observed. Hence, 1:1:1 molar ratio was the minimum requirement for the effective one pot synthesis of triazoles. It was also noticed that further increase in the molar ratio did not have any considerable effect on the conversion percentage.

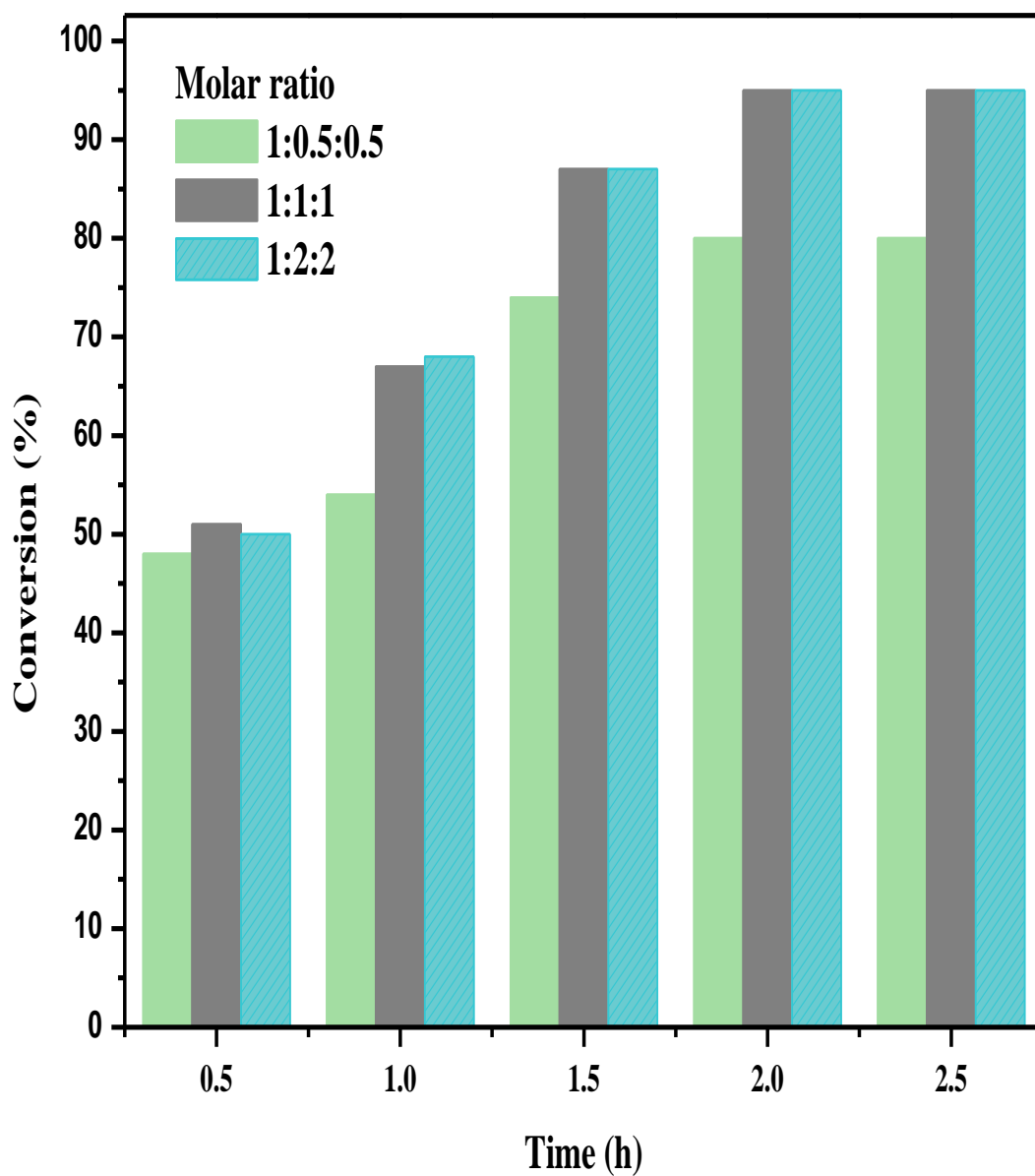


Fig. 5.8: Effect of amount of catalyst on the model reaction (Reaction conditions: phenyl acetylene (a mmol), benzyl bromide (b mmol) and sodium azide (c mmol), catalyst (20 mg), water/^tBuOH (2 mL), stirring at 55°C).

Further, effect of variety of bases such as K_2CO_3 , NaOH, NEt_3 , DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) and NaOAc have been investigated on the model reaction. Out of all the bases tested, NaOAc was found to be superior in terms of

obtained conversion percentage as shown in Table 5.3. K_2CO_3 and DBU gave only low to moderate yields, while no reaction was observed in the presence of NEt_3 and NaOH.

Table 5.2: Effect of various bases on oxidative amination of aldehydes^a

Entry	Base	Conversion ^b (%)	TON(TOF) ^c
1.	K_2CO_3	5	45(15)
2.	NaOH	49	445(148)
3.	NEt_3	56	509(167)
4.	DBU	89	809(270)
5.	NaOAc	97	882(294)

^a Reaction conditions: phenylacetylene (1 mmol), base (1 mmol) acetonitrile (2 mL) and $SiO_2@APTES@SAL-Cu$ catalyst (20 mg), room temperature, 3 h.

^b Conversion and yield were determined by GC-MS.

^c TON is the number of moles of product per mol of catalyst and TOF = TON per hour.

Solvent also plays a crucial role on the efficacy of SiO₂@APTES@SAL-Cu catalyst in oxidative homocoupling of terminal alkynes. Hence, the selected model reaction was carried out in presence of various solvents and the results are summarized in Figure 5.9. It was found that when chloroform and toluene were used, negligible conversion was observed. However, polar aprotic solvents like DMSO, acetonitrile, THF, DCM and DMF favoured the activity of SiO₂@APTES@SAL-Cu heterogeneous catalyst for the alkyne homocoupling. It can be seen that, maximum conversion was observed when acetonitrile was used as a solvent.

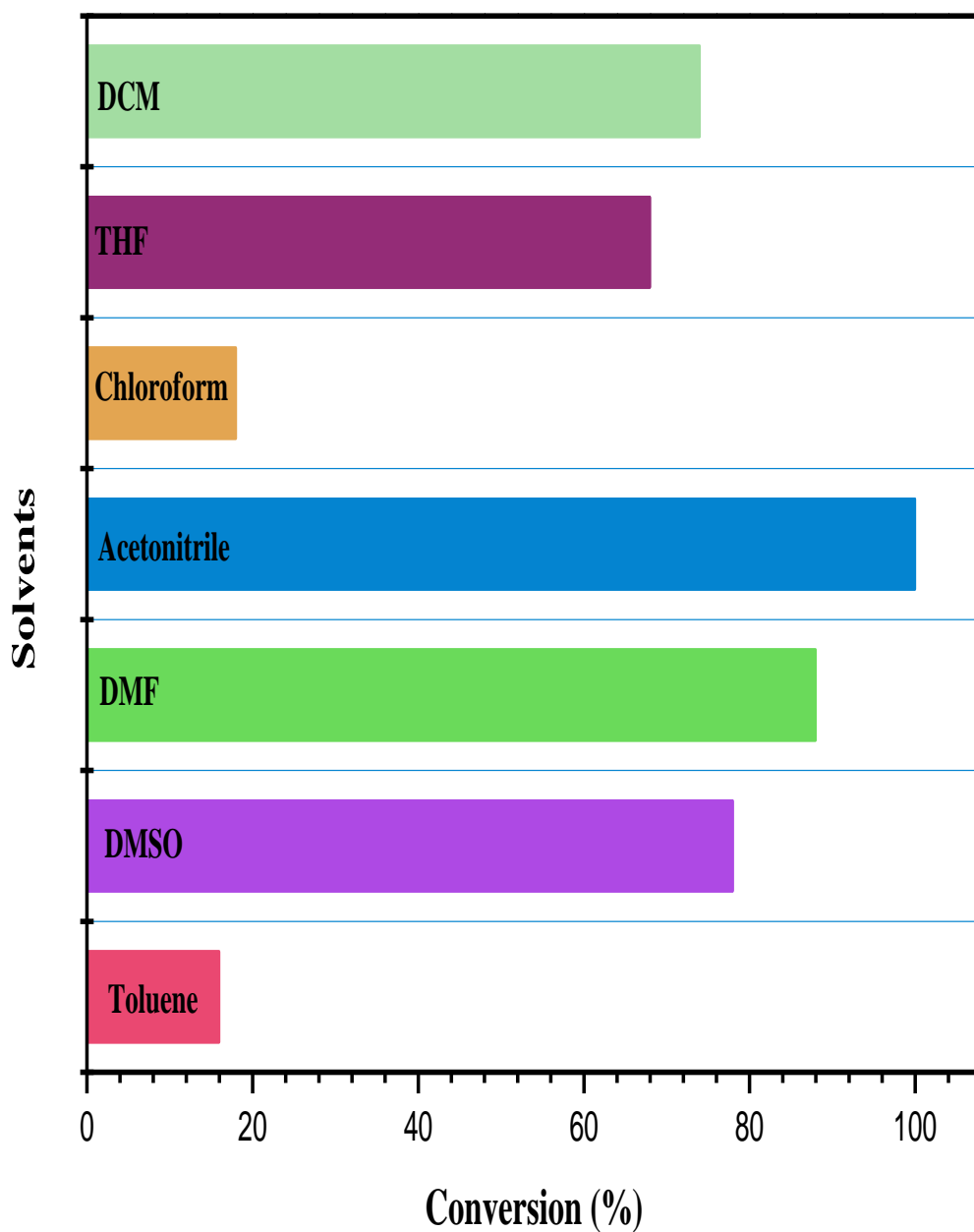
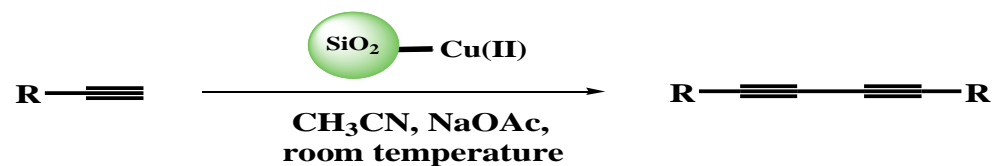


Fig. 5.9: Effect of solvent on the catalyst efficacy of SiO₂@APTES@SAL-Cu (Reaction conditions: phenylacetylene (1 mmol), NaOAc (1 mmol) solvent (2 mL) and SiO₂@APTES@SAL-Cu catalyst (20 mg), room temperature, 3 h).

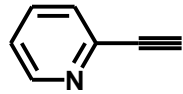
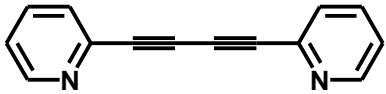
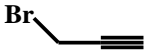
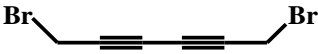
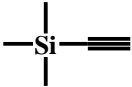
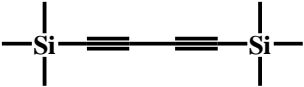
In order to understand the scope and generality of the reaction, a wide range of acetylenes were subjected to the oxidative homocoupling of terminal alkynes

under the optimized reaction conditions. The reactions of aromatic alkynes with both an electron-withdrawing group and an electron-donating group proceeded well with higher conversion percentage in presence of SiO₂@APTES@SAL-Cu (Table 5.3). Further, the present catalytic system was applied successfully for the homocoupling of aliphatic terminal alkynes. However, when aliphatic acetylenes were used, the yields were somewhat lower. This may be attributed to less reactivity of aliphatic terminal alkynes towards homocoupling reaction, probably due to the weaker acidity of the acetylenic proton.

Table 5.3: SiO₂@APTES@SAL-Cu catalyzed oxidative homocoupling of terminal alkynes ^a.



S.No.	Terminal alkyne	Product	Time (h)	Conversion b (%)	TON (TOF) ^c
1.			3	100	909(304)
2.			2.5	99	900(360)
3.			3	99	900((300)
4.			2.5	100	909(364)
5.			3.5	98	891(255)

6.			4	83.5	759(188)
7.			6	64	582(97)
8.			3.5	99	900(257)

^a Reaction conditions: terminal alkyne (1 mmol), NaOAc (1 mmol) acetonitrile (2 mL) and SiO₂@APTES@SAL-Cu catalyst (20 mg), room temperature.

^b Conversions were determined by GC-MS.

^c TON is the number of moles of product per mol of catalyst and TOF = TON per hour.

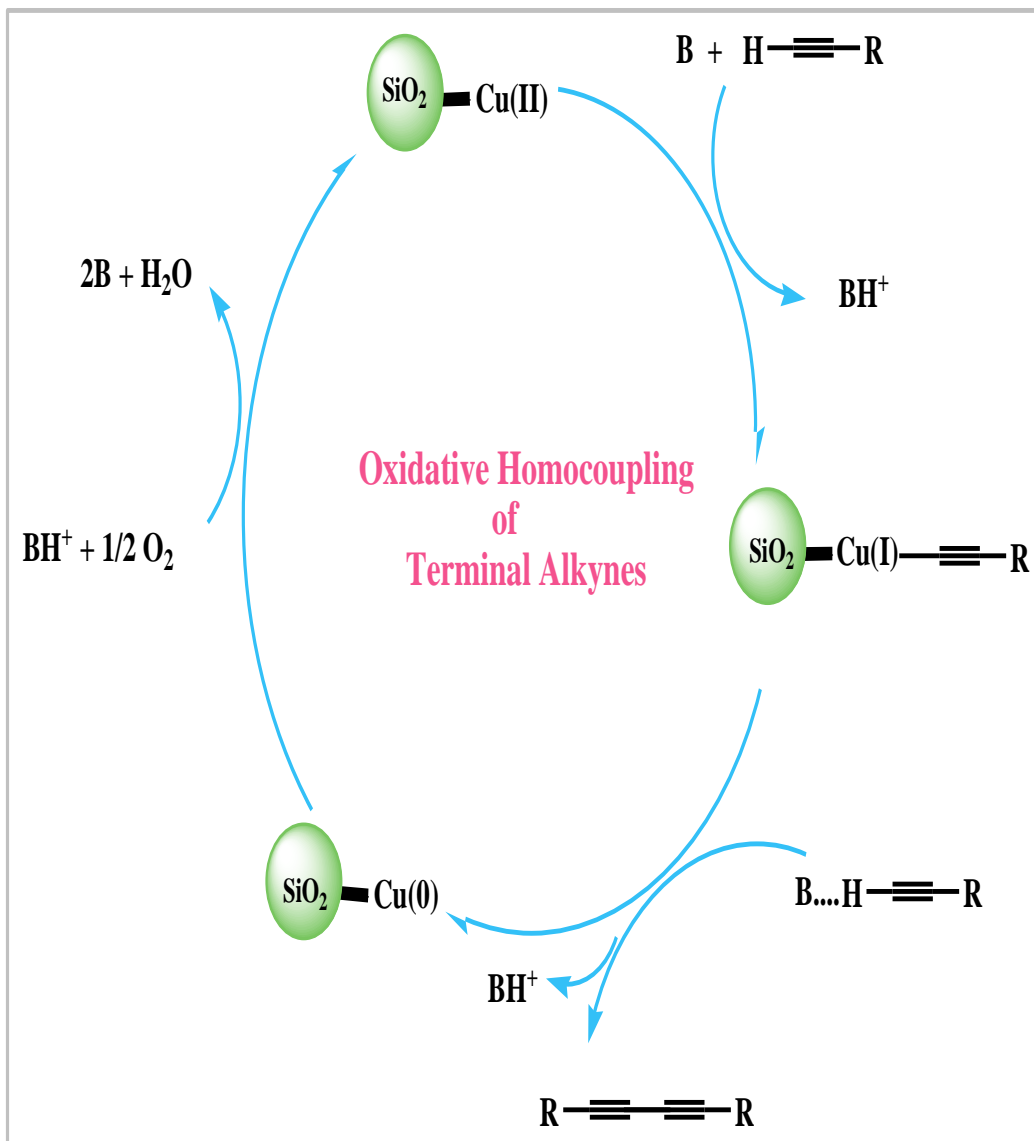


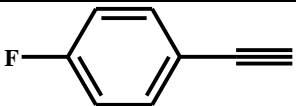
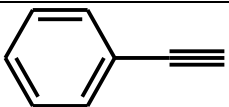
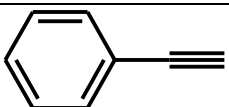
Fig. 5.10: Probable reaction mechanism of SiO₂@APTES@SAL-Cu catalyzed oxidative homocoupling of terminal alkynes.

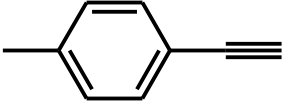
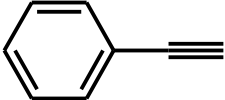
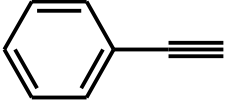
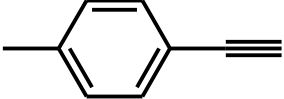
Further, a plausible mechanism for oxidative homocoupling of terminal alkynes has been proposed as shown in Figure 5.10. The catalytic cycle starts via insertion of the C–H bond of the terminal alkyne promoted by Cu(II) species in combination with base NaOAc which leads to generation of a Cu(I) acetylide

intermediate. The Cu(I) species thus formed get reduced to Cu(0), resulting in the formation of the 1,3-diyne coupling product.

Table 5.4 presents the literature precedents of metal catalyzed oxidative homocoupling of terminal alkynes under different reaction conditions and the results have been compared with those obtained by using SiO₂@APTES@SAL-Cu as catalyst (Table 5.4). It is evident that the organic–inorganic hybrid catalyst (SiO₂@APTES@SAL-Cu) shows good results in terms of the reaction conditions and product yield in comparison to reported catalysts in literature so far.

Table 5.4: Comparison of the catalytic activity of SiO₂@APTES@SAL-Cu catalyst with some recently reported catalysts in literature for oxidative homocoupling of terminal alkynes

Entry	Terminal alkyne	Catalytic system	Reaction conditions	Yield	Ref.
1		SBA-15@DABCO-Pd	DABCO, CuI, CH ₃ CN, room temperature, 24 h.	94	46
2		Cu(II)-Clay	DMSO, room temperature, 25 min	98	47
3		CuI	NaOAc, DMF, 90°C, 30 h	97	48

4		CuSO ₄ ·5H ₂ O	KOAc, I ₂ , H ₂ O, 120 °C, 24 h	93	49
5		Cu(OAc) ₂ ·H ₂ O	DMSO, air, 90°C, 10 h	90	50
6		CuBr	di- tertbutyldiaziridin one, CuBr , CH ₃ CN	80	51
7		Cu(II)-SBA- 15	DMSO, 100°C, 2 h	97	52

5.3 REUSABILITY AND HETEROGENEITY TEST

In order to determine the true heterogeneous nature of Cu species in our catalytic system, additionally a hot filtration test was carried out. For that, the solid catalyst was filtered out after the oxidative homocoupling of phenyl acetylene had run for 2 h (conversion 45%). The solid-free filtrate was then transferred to another reaction vessel and continually stirred under standard reaction conditions. After 12 h, GC results revealed that after separation of the catalyst no conversion takes place in the filtrate part. This confirmed that the reaction did not proceed after the removal of the catalyst. Further, no evidence for leaching of copper or decomposition of the complex catalyst was observed which was further confirmed by atomic adsorption analysis of the filtrate solution that showed any copper

content within the detection limit (less than 1 ppm). These studies clearly demonstrated that copper was intact to a considerable extent with the heterogeneous silica support, and there is no significant amount of leaching occurred during reaction.

Recycling and life time of the heterogeneous catalysts are significant issues for practical applications. Hence, reusability of our supported catalyst was investigated in the oxidative homocoupling of phenyl acetylene under the optimized reaction conditions. After completion of the reaction, the catalyst was recovered and washed with ethyl acetate and dried under vacuum. The recovered catalyst was employed in the next run. It is evident from Figure 5.11. The recycled catalyst did not show any appreciable change in the activity after five cycles indicating that the catalyst is stable and can be regenerated for repeated use.

Solid support material is to enhance the lifetime of the resultant catalyst thereby rendering it suitable for industrial applications. In order to investigate the reusability of the $\text{SiO}_2\text{@APTES@2HAP-Cu}$ catalyst, the model reaction was performed under the optimized reaction conditions. Upon completion of the reaction, the catalyst was separated by filtration after each run, dried under vacuum and then subjected to the next reaction cycle under the same conditions. It is well evident from Figure 5.11 that there was no remarkable decrease in conversion percentage even after six runs indicating the excellent durability and

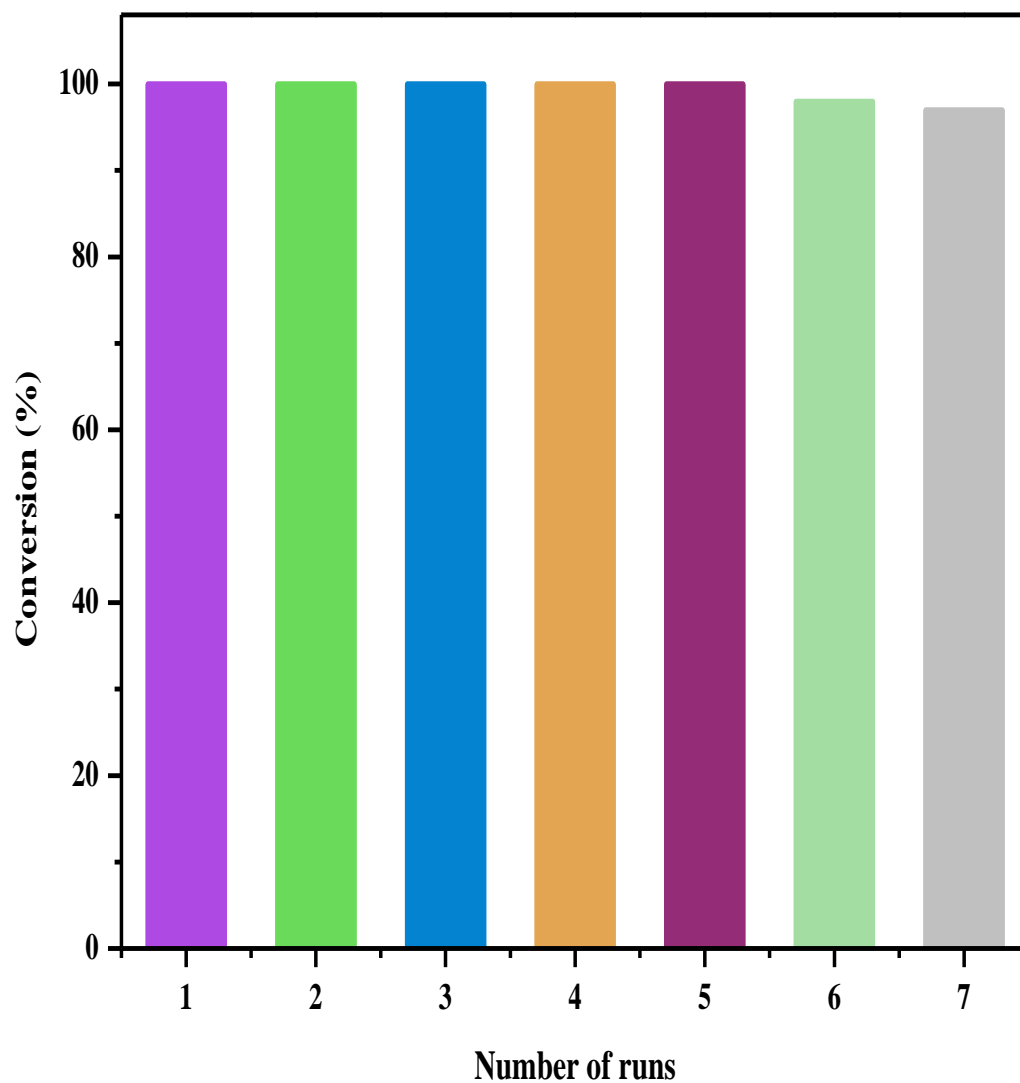


Fig. 5.11: Catalytic reusability test for oxidative homocoupling of terminal alkynes (phenylacetylene (1 mmol), NaOAc (1 mmol) acetonitrile (2 mL) and SiO₂@APTES@SAL-Cu catalyst (20 mg), room temperature, 3 h).

One of the main reasons for immobilizing homogeneous metal complexes onto reusability of the synthesized catalyst. In addition to this, FTIR and SEM analysis of the reused catalyst after sixth run was also carried out. It was found that there was no significant difference in the FTIR patterns and SEM images of the fresh

and the reused catalyst which provided a concrete evidence for the good structural stability of SiO₂@APTES@2HAP-Zn under the employed reaction conditions.

CHAPTER 6:

CONCLUSION

CHAPTER 6

CONCLUSION

In conclusion, a novel silica based organic-inorganic copper catalyst was successfully synthesized via covalent immobilization of salicylaldehyde onto amine functionalized silica gel followed by metallation with copper acetate. The prepared catalyst was found to be highly effective for oxidative homocoupling of terminal alkynes as compared to those of previously reported catalysts. Moreover, it also displayed excellent stability and could be repeatedly reused five times without any significant loss in its catalytic efficacy. The major advantages of the synthetic protocol are mild reaction conditions, short reaction time, high yields, preparation of the catalyst from commercially available starting materials, easy recovery and recyclability of the catalyst which makes this protocol a valid candidate towards the goal of green chemistry.

A novel, highly efficient and reusable silica based organic-inorganic hybrid copper catalyst ($\text{SiO}_2\text{@APTES@SAL-Cu}$) has been synthesized via covalent bonding of salicylaldehyde onto amine functionalized silica gel followed by metallation with copper acetate and it was found to be highly effective for oxidative homocoupling reactions of terminal alkynes. The synthesized catalyst was characterized using several techniques such as Scanning electron microscopy (SEM), ^{13}C CPMAS NMR spectroscopy, Fourier transform infrared (FT-IR)

spectroscopy, elemental analysis, Brunauer–Emmett–Teller (BET) surface area analysis, Energy dispersive X-ray fluorescence spectroscopy (ED-XRF), Atomic absorption spectroscopy (AAS) and X-ray diffraction (XRD) studies. The alkynes coupling was investigated with phenyl acetylene as test substrate. The work-up procedure is very simple and products were obtained in moderate to high yields. The catalyst can be recycled and reutilized further for various catalytic reactions. The drive towards clean technology in the chemical industry and the emergence of green chemistry related issues in chemical research and education are unlikely to be short term ‘fashions’. In the future, the synthetic chemist will need to be as concerned about atom efficiency as the synthetic route and the process chemist will need to be as concerned about the waste produced as the product to be made. It is already becoming evident that the more successful chemical manufacturing companies of the future will be those that can exploit the economic, legislative and public image advantages that a clean technology approach to chemical manufacturing can provide. Also, the more successful chemistry researchers and educationalists will be those that can appreciate the value of green chemistry in innovation, application and teaching (as well as recognising the important role that green chemistry can play in enhancing the attractiveness of chemistry as a discipline).

In summary, we have developed a silica based organic-inorganic hybrid copper catalyst ($\text{SiO}_2\text{@APTES@2HAP-Cu}$) of unprecedented activity and recyclability through the covalent immobilization of 2-hydroxyacetophenone on the surface of the amine functionalized silica support followed by its metallation with copper

chloride. The resultant heterogeneous catalytic system exhibits remarkable efficiency in terms of excellent product yield and high turn-over number in the synthesis of 1,4 disubstituted 1,2,3 triazole derivatives. The hot filtration test ensures that the catalyst works in a heterogeneous manner and is devoid of leaching problem.

The facile recovery, coupled with the intrinsic stability of the support material allows the catalyst to be recycled over six times without any discernible loss in its activity. Besides, simple procedure, solvent free reaction conditions, ambient temperature and economic feasibility are some of the additional attributes of the present protocol that render it highly suitable for addressing various economic and industrial concerns.

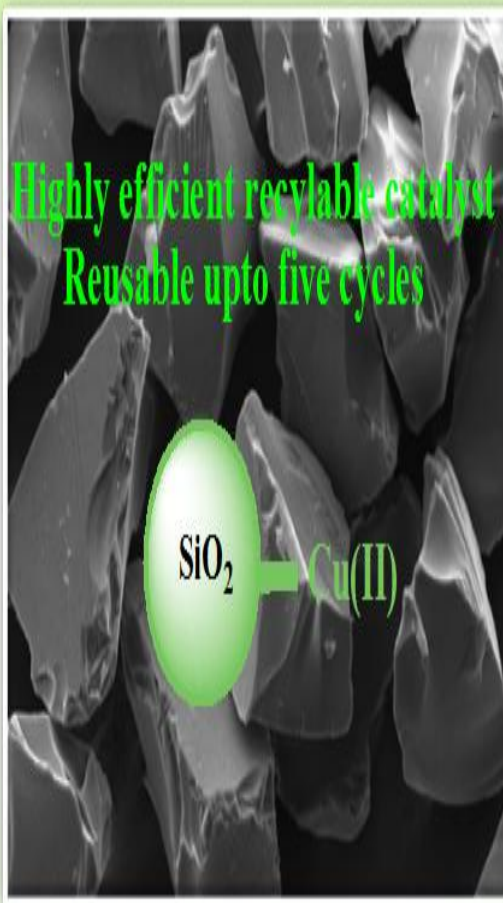
Copper complex was covalently anchored onto the surface of amine functionalized silica gel, and its catalytic efficacy was investigated for oxidative homocoupling of terminal alkynes. The features of mild reaction conditions, simple work-up procedure, excellent product yield, high turn-over frequency (TOF), easy recovery and reusability of the catalyst are the significant advantages of the present protocol.

While many exciting new greener chemical processes are being developed it is clear that a far greater number of challenges lie ahead. In two of the largest generic areas of chemistry, acid catalysis and partial oxidations, there are countless processes operated by almost every type of chemical manufacturing company, producing products of incalculable value yet also producing almost immeasurable volumes of hazardous waste. New greener chemistry is needed.

One of more important development areas in this context will be the more widespread use of heterogeneous catalysis in liquid phase organic reactions.

The enormous range of reactions and the rapidly growing number of new catalysts will require the use of rapid screening methods and those of innovative engineering to fully exploit the new chemistry. Synthetic chemists must be more prepared to work with catalyst chemists who must in turn work more closely with chemical and process engineers. For every challenge offered by the green chemistry revolution there is also an exciting opportunity.

**OXIDATIVE
HOMOCOUPLING
OF TERMINAL
ALKYNES**



- Excellent product yield
- High Turnover number
- Mild reaction conditions
- Economical
- Easy workup procedure
- Recyclable and reusable catalyst



Fig. 6.1: Overview of work

CHAPTER 7:

REFERENCE

CHAPTER 7

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14+ YEARS OF EXPERIENCE IN ANALYTICAL RESEARCH AND QUALITY ASSURANCE

QUALITY MANAGEMENT SYSTEMS ⇒ AUDITS ⇒ QUALITY RELATED DOCUMENTATIONS
⇒ TECHNOLOGY TRANSFER DOCUMENTS ⇒ SOP'S MANAGEMENT ⇒ VENDOR
MANAGEMENT ⇒ QUALITY BY DESIGN ⇒ GAP ANALYSIS ⇒ CALIBRATION OF
INSTRUMENTS ⇒ SYSTEMS ESTABLISHMENTS ⇒ LEADERSHIP QUALITIES ⇒ ANALYTICAL
THINKER & PROBLEM SOLVER ⇒ EXPERTISE IN METHOD DEVELOPMENT ⇒ METHOD
VALIDATION ⇒ CHARACTERISATION ⇒ INSTRUMENT HANDLING

Resourceful professional skilled in designing, developing and executing quality assurance and control processes, test strategies, test plans; skilled in featuring design documents, as well as application standards. Adept in selecting the testing methodologies with focus on latest automation technologies - Accountable for Quality assurance of other non-functional areas such as performance, training, installation / upgrade etc

CAREER EXPOSURE: *Vyome Biosciences, (Sr. Manager_QA & Analytical) Fresenius – Kabi Oncology (Assist Manager QA), Senior Research Scientist – II in Analytical Department of DaburPharma, Senior Research Chemist Ranbaxy Research Laboratories*

KEY CAREER MILESTONES / BENCHMARKS

KEY TECHNICAL SKILLS

- Expertise in analytical method **development, method validations, Pharmacopeia** monographs evaluations, **method transfer** and evaluate the quality and shelf life of API and drug product. Holds the credit of handling multiple projects in the same time delivering quality outcomes within timelines and budget.
- Analytical support and involvements investigation of product complaints and timely reply to all the complaints.
- Resolved analytical issues during analytical method development/ validations and routine analysis of various APIs and formulations by using state of art trouble shooting techniques.
- Expertise in HPLC, GC, MS-MS, DSC, TGA, Dissolution, UV, wet analysis, AAS, Residual solvents, Metal estimation Drug retention, Chiral separations, Regulatory queries, Bioequivalence studies, Thermal studies, Stability studies & Validations.
- Highly analytical with excellent problem solving skills and impeccable leadership abilities.

Established and implemented current GXP – GLP, GMP, GCP, AND GDP Systems being the founding member of the Development Quality assurance at Vyome Biosciences Limited

Successfully worked for USFDA audit in R&D of FKOL, handled two – day QMFK Audits, Internal audits, and faced ISO Pre Audit

Maintained 100% compliance of GLP norms in Ranbaxy Research Laboratories, Maintained Mass Instruments, LC, LCMS

Skilled in working of Gas Chromatography, HPLC, DSC, TGA and FTIR, UPLC

Served as Management Representative and led Fresenius – Kabi Oncology Limited as ISO 9001: 2008 in March 2013

An expert in performing preventive maintenance of all instruments and conducting their calibrations precisely

An effective leader with excellent communication and motivation skills and mastery in conflict resolution, Played a crucial role in developing the skill sets of team members and inspired them for performance excellence by implementing motivational initiatives.

MANAGERIAL EXPERTISE

Strategy & Planning

- ✓ Develop and establish quality assurance measures and testing standards for new applications, products, and/or enhancements to existing applications throughout their development/product lifecycles
- ✓ Prepare and deliver reports, recommendations, or alternatives that address existing and potential trouble areas in systems and projects across the organization

Acquisition & Deployment

- ✓ Liaise with vendors and suppliers in assessing applications and/or systems under consideration for purchase.
- ✓ Analyze documentation and technical specifications of any new application under deployment or consideration to determine its intended functionality

Operational Management

- ✓ Conduct internal audits to measure and assure adherence to established QA standards for research development, application integration, and information system performance, and corresponding documentation
- ✓ Create and execute test plans and scripts that will determine optimal application performance according to specifications.
- ✓ Verify and revise quality assurance standards as needed
- ✓ Ensure that testing activities allow applications to meet business requirements and systems and goals, fulfil end-user requirements, and identify existing or potential issues
- ✓ Collaborate with software/systems personnel in application testing, such as system, unit, regression, load, and acceptance testing methods
- ✓ Make recommendations for improvement of applications to programmers and software developers or engineers
- ✓ Communicate test progress, test results, and other relevant information to project stakeholders and management
- ✓ Test any new software to ensure integration into company systems meets functional requirements, system compliance, and technical specifications
- ✓ Analyze formal test results in order to discover and report any defects, bugs, errors, configuration issues, and interoperability flaws
- ✓ Assist in the development of change control processes, practices, and guidelines for new and existing technologies
- ✓ Participate in developing, distributing, and coordinating in-depth end-user reviews for modified and new systems or applications
- ✓ Cultivate and disseminate knowledge of quality assurance best practices

PROFESSIONAL CAREER HISTORY

VYOME BIOSCIENCES LIMITED, DELHI, OCTOBER 2011 ONWARDS

Designation: Sr. Manager – Analytical Development and Quality Assurance (Oct 2013 to till date)

Manager Analytical Development and Quality Assurance (Oct 2011 to Sep 2013)

Reporting Line: Sr. Vice President R&D and CEO

About Company: Vyome Biosciences is one of the first innovation driven Research and Development Companies in India. Eminent scientists from both India and abroad founded the company and making it the most exciting and happening place in dermatology. The company is developing new generation of therapeutics to treat various dermatology indications using its novel technology platforms. The board consists of leaders from the field of science, technology and finance. The company focuses on developing novel and break through treatments for hard to treat and refractory skin conditions such as persistent dandruff and skin fungal infections, resistant acne and other skin bacterial infections.

KEY HIGHLIGHTS

- Provided Leadership to the Analytical development and Quality Assurance departments simultaneously
- Successfully implemented Quality System in entire R&D and accountable for Quality by Design
- Key person to develop, implement and review the Quality Management System and ensure regulatory requirements are met and adhered to quality laboratory practices
- Led Analytics to extend guidance and attain expertise in analytical method development of different dosage OTC and Pharma products like Emugel, creams. Analytical is working on differentiated products and innovative commercialization strategies.
- Performed review and evaluation of analytical methods supporting the validation and development activities.
- Proactively plan new product development of specified consumer(OTC products, antifungal, antibacterial treatment, treatment of diabetic ulcer and treatment of skin pigmentation disorders).Handling all the analytical issues at the outsourced manufacturing locations and which led to successful product launch.
- Developed Standard Operating Procedures, method assessments product specifications, test methods etc.
- Conducted technical documentation reviews for laboratory notebook, protocol and reports.
- Spearheaded regular analysis of various synthesis groups, checked the product quality as per specifications and functioned as a critical member in the R&D Lab Development.
- Designed experiment, planned and executed the recipes, batch specifications, cost calculations etc.

KEY ACCOMPLISHMENTS REGARDING PATENTS FILED

- ✓ Topical Oil compositions for treatment of fungal infections – Application Number 3746 / DEL/ 2011 – 20.12.2011
- ✓ Conjugate based antifungal and anti-bacterial prodrugs – Application Number – WO 2012 / 177986 A2 – International Publication Number – 22.06.2012
- ✓ Awarded by the company for successful implementation of ISO 9001:2008 and implementing quality from scratch.

FRESENIUS – KABI ONCOLOGY LIMITED, GURGAON, OCTOBER, 2009 - 2011

Designation: Assistant Manager – Global Quality Assurance in Innovation and Development

Reporting Line: General Manager

KEY HIGHLIGHTS

- Successfully implemented work instruction/documentations and SOP's / WIs / GDs related to QA and other departments
- Key person to conduct training of new employees related to Quality assurance Systems in FKOL
- Handle the specifications review, testing methods, manufacturing instructions, master batch records, stability studies, methods and process validation studies
- Handle the processing of change controls related to FKOL documents
- Ensured compliance with cGMP and regulatory regulations
- Key person to handle the GAP analysis and impact analysis for audits
- Prepared CAPA and its implementation in R&D; Conducted quarterly QMFK circular updation in R&D
- Completely overseeing the project management and delivering the same on-time and within budgets and assessing the risk assessment
- Conduct the vendor agreements of primary packaging material along with vendor selections

DABUR RESEARCH FOUNDATION, DELHI, OCTOBER, 2007 - 2008

Designation: Senior Research Scientist – II in Analytical Department

Reporting Line: Assistant Director

KEY HIGHLIGHTS

- Qualitative and Quantification of API via HPLC(Assay, related substances, reaction monitoring, Franz, drug release studies etc)
- Residual solvents determination via Head Space Gas Chromatography
- Molecular Weight Determination via LCMS
- Handling of regulatory Queries
- Analysis of Stability, Thermal, Chemical, Moisture, Elemental analysis
- STP and Specifications Finalization
- Technology Transfer at Manufacturing Locations
- Method Validation – Assay, Related Substances and Residual Solvents

RANBAXY RESEARCH LABORATORIES LIMITED, GURGAON, 2000 – 2007
Designation: Senior Research Chemist – 2004 – 2007 / Research Chemist – 2000 – 2002
 Reporting Line: Associate Director/Group Leader

KEY HIGHLIGHTS

- Responsible for all aspects of analytical analysis required for the API (bulk drugs) Routine, Characterization, Method Development Group (developing various methods for HPLC, GC, i.e. assay methods, related substances, residual solvents, chromatographic purity, chiral enantiomeric separation by reverse phase and normal phase methods). HPLC, Residual solvent method for GC and GCMS, maintaining working standards and following GLP. Elemental analysis by AAS (Atomic Absorption Spectroscopy)
- Worked for five and a half years in the R&D of Ranbaxy Research Laboratories Ltd, with three-and-a-half years in the New Drug Discovery Research. Conducted complete analytical analysis of NCEs (API), (routine study, stability study, validation method development). Mass direct as well as LCMS in single quadrupole and triple quadrupole, GC, HPLC, DSC, TGA

PROFESSIONAL SCHOLASTICS

- **Bachelor of Applied Sciences in Instrumentation (Hons.) from Delhi University - RANK-HOLDER IN THE UNIVERSITY**
- **Masters in Environment Chemistry from Jiwaji University – TOPPED THE UNIVERSITY**
- ✓ **Semester I:**
Fundamentals of Quantitative Analysis & Separation Method, Data Evaluation and Thermo Analytical Methods, Spectro Analytical Method of Analysis, Electro Analytical Methods of Analysis
- ✓ **Semester II:**
Spectrochemical Methods of Analysis, Computer in Chemical Analysis, Elementary Electronics in Chemical Instrumentation, Environment and Pollution Control
- ✓ **Semester III**
Industrial Waste and Water Treatment, Environment Toxicology and Environment, Impact Assessment Energy and Environment, Geochemistry, Environment Laws and Management
- ✓ **Semester IV : Industrial Training**

{TOPPED IN ALL FOUR SEMETERS WITH 86%}

Pursuing part time PhD from University of Petroleum and energy studies. Coursework, synopsis & abstract approved

Research Topic: Study and development of “Recyclable and reusable silica based organic – Inorganic hybrid catalyst “A concept of Green chemistry Lab work performed at Green Chemistry Network Centre - Delhi University

Course work cleared, Synopsis approved, Abstract approved Thesis completed, Ready for thesis submission.

Papers, reviews and posters

Presented poster on the **International workshop** on "Green Initiatives in Energy, Environment and Health" sponsoring by **High impact Royal Society of Chemistry (RSC)** latest impact factor is **6.828** on Dec 2 and 3 of 2013.

Title of the poster

Silica based organic inorganic hybrid catalysts for diverse organic transformations bridging the gap between homogenous and heterogeneous catalysts.

Title of the papers :

An efficient, reusable, recyclable silica based organic-Inorganic hybrid copper catalyst for homocoupling of terminal alkynes. Accepted in "**International journal of chemistry**"

Silica supported organic inorganic hybrid catalyst_ A concept of green chemistry" accepted in **International Journal of Green Chemistry.**

Organic-Inorganic hybrid silica based copper complex as a novel and highly recyclable heterogeneous catalyst for cross dehydrogenative coupling reaction of amines with formamides communicated at **Journal of molecular catalysis. A**

Zinc (II) complex immobilized on amine functionalized silica gel: A novel, highly efficient and recyclable catalyst for multicomponent click synthesis of 1,4-disubstituted 1,2,3-triazoles communicated at **Journal of coordination chemistry**

A **Review** on Challenges and Opportunities in Green Pharmacy accepted in "International Journal of Green chemistry".

Conferences: Participated in **5th Asia Oceania conference on Green and sustainable chemistry** 15 to 17 Jan 2015 in New Delhi.

TRAININGS RECEIVED

Trainings in the Analytical:

- 2006 - **MASS, MS-MS, LCMS, and UPLC** training organised by Waters in **Singapore**
- Participated in Poster Presentation on Chiral Separations in Annual Med Chem Symposium at Ranbaxy in 2006
- Two months of summer job with Dabur Research Foundation in Analytical Department. The project was: Modern Instrumentation and Chemical Techniques Used in Industrial Analysis
- Two months of summer training with Ranbaxy Research Lab's Analytical Department in 2000 - exposed to Routine Analysis by being a part of the Formulations Group
- Two months of summer training with Shriram Institute of Industrial Research in 1999. Worked with the micro-bio lab, pesticide lab, drug lab, instrumentation lab, and mineral and ore lab.

Trainings in the Quality Assurance:

- Safety Training conducted by safety officer of API plant in Kalyani
 - Two days of training on the review of Verification and Validations by the United State Pharmacopeia in Hyderabad
 - Two days training on Good Quality Control Laboratory Practices, with the emphasis on new schedule L1 GLP in Mumbai
 - Certified internal auditor
 - Qbd : An indispensable tool for "Pharma Product Development" excellence and regulatory compliance.
 - Six sigma green belt by Indian Statistical institute Delhi
- ✓ Participated in 42nd Annual National Conference of IADV (Dermacon 2014) & XI International congress of Dermatology and presenting posters of two projects of our company along with cross functional teams on December 05th 2013

- ✓ Interviewed by a leading TV channel about Instrumentation course and its career aspects of Delhi University

PERSONAL DOSSIER

- Date of birth: September 16th 1979
- Address: SF – 66, Vardan Apartment, Module – 19&20, Abhaykhand – III, Indirapuram, Ghaziabad
- Languages: Hindi, English, Punjabi
- Interests: Debates, Declamation – English, Hindi, Recitation, Acting, Painting, Creative Writing
- Conducted various programs on sciences for All India Radio