ORGANIC SYNTHESIS MEDIATED BY HETEROGENEOUS CATALYSTS

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Doctor of Philosophy

in

Chemistry

Under the Faculty of Science

by

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Certificate

This is to certify that the thesis entitled **"Organic Synthesis Mediated by Heterogeneous Catalysts"** submitted for the award of the Degree of Doctor of Philosophy of the Cochin University of Science and Technology, is a record of original research work carried out by Mr.Kannan. V, under my supervision and guidance in the Department of Applied Chemistry, and further it has not formed the part of any other thesis previously.

Kochi-22
9th August 2011

Dr.K.Sreekumar
(Supervising Teacher)

DECLARATION

I hereby declare that the thesis entitled **"Organic Synthesis Mediated by Heterogeneous Catalysts"** submitted for the award of Ph.D. Degree of the Cochin University of Science and Technology, is based on original research work done by me under the guidance of Dr.K.Sreekumar, Professor and Head, Department of Applied Chemistry, Cochin University of Science and Technology and further that it has not previously formed the basis for the award of any other degree.

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9th August 2011

Kannan V.

"When you look at yourself from a universal standpoint, something inside always reminds or informs you that there are bigger and better things to worry about".

Albert Einstein

Dedicated To My Father

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Preface

The science and practice of catalysis is central to most activities in chemical industry. Catalysis is probably one of the most ancient chemical phenomena, claiming many early molecules were formed by catalytic process involving metal or photocatalysis. In recent years, catalysis has become an important route to the improvement of environmental quality by helping in the abatement of air pollution and the reduction of industrial waste.

The use of clay for making clay figures, pottery and ceramics has been known about 25,000 years ago. Later it has found application in the use of ceramics, oil drilling, metal and paper industry. They are also used as adsorbents, decolorizing agents, ion exchangers and as catalysts. Currently the use of clays in organic synthsesis is increasing due to their non corrosive nature and ease of separation after reaction and low cost. Various forms of clays have been employed for this purpose.

The present work is oriented to synthesize clay modified catalysts by various methods such as wet impregnation, pillaring, ion exchange etc.

The thesis is structured into seven chapters. First chapter deals with a brief introduction on clays, their structure, classification, properties, various methods of modifications and literature survey on clays. Second part of the first chapter describes a brief literature survey of organic reactions such as addition, condensation, isomerisation, oxidation etc catalysed by clays. Objectives of the present work and materials and methods used in this work are given at the end of the chapter.

Second chapter starts with the preparation of montmorillonite K10 clay supported titanium catalyst by wet impregnation method. The catalyst characterization by XRD, SEM, UV-DRS, FTIR, AES and TG are described. The catalyst has found application in the solvent free synthesis of

tetrasubstituted imidazoles and some theoretical aspects of substitution effects are given. The catalyst is also effective for the synthesis of Mannich bases which is given at the end of this chapter.

Pillaring is one of the widely used methods of modification of clays to improve the catalytic activity by increasing the interlayer distance. The preparation of aluminium pillared saponite clays are discussed followed by its characterization and application for the synthesis of cyclic acetals of pentaerithritol. Various factors which control the reaction and mechanism of formation of cyclic acetals are given in this chapter.

Bimetallic catalysts are more effective than monometallic catalysts in many reactions. The preparation and characterization of Pd-Cu exchanged KSF and Pd-Co exchanged montmorillonite KSF are discussed in the first part. The second part consists of catalytic application of the prepared catalyst in Heck-Coupling and Suzuki-Coupling reactions. Their mechanism and various factors which control the reactions are given in chapter four.

An attempt was made to prepare heterogeneous version of chiral catalyst was made in chapter five. Preparation of clay supported chiral dipeptide metal complex catalysts; their characterization and use in Aza-Diels Alder reaction are discussed in chapter five.

Microwave irradiation, an unconventional energy source, has been used for a variety of applications including organic synthesis. Sixth chapter deals with the catalyst assisted solvent free synthesis of triarylpyridines, and synthesis of benzimidazoles under conventional and microwave assisted conditions

Last chapter comprises the summary of the investigation and the conclusions drawn from the earlier chapters.

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Chapter 1

INTRODUCTION AND LITERATURE SURVEY

Contents

Heterogeneous catalysis is crucial to chemical technology. Innumerable chemical reactions are facilitated by catalysts. Chemical bonds are broken and new chemical bonds are formed during the catalytic process. These events occur repeatedly, usually without a significant change of the catalyst. In the absence of the catalysts, chemical transformations would either not occur or would take place with lower efficiencies or slow rates. A brief introduction on clays, their structure classification and properties has been described. A review of organic reactions mediated by clay catalysts and objectives of the present work are presented in this chapter

1.1 Introduction

The first period of catalysis dates back to the dawn of civilization, at a date lost in time when mankind began to produce alcohol by fermentation.

This period of catalysis ended stridently when Jöns Jacob Berzelius systematically investigated the recorded observations and classified them as catalysis in 1835 [1]. The new perception of catalysis was clearly formulated by Wilhelm Ostwald, who once wrote that "there is probably no chemical reaction which cannot be influenced catalytically". Catalysis has wide ranging applications in chemical industry and has a major impact on the quality of human life as well as economic development. Catalysis is also looked upon as a solution to climate change or replace polluting processes due to inherent characteristics of most catalytic processes as clean technologies [2]. The production of most of the chemical products available in the market is based on chemical processes which involve catalysis.

1.1.1 Heterogeneous catalysis

Catalysis is broadly divided into homogeneous and heterogeneous catalysis. Homogeneous catalytic reaction is one in which the reactants and catalyst are in the same phase and if the reactants and catalysts are in different phases, it is heterogeneous catalysis. Each of these has its own advantages and disadvantages. Homogeneous system offers better selectivity, activity as compared to heterogeneous catalysts; the disadvantages of homogeneous catalysts are low thermal stability and short life time. The advantage of heterogeneous catalytic process is the easy separation of catalyst after the reaction, reusability and possibility of continuous operation in a reactor without intrerruption. Heterogenous processes are more environmentally friendly.

Phenomenal growth in the use of inorganic solids as reaction media for organic transformations is an important area of research [3-6]. Lazlo et al. even went on to claim that the future of synthetic organic chemistry rests with heterogeneous media rather than the currently predominant homogeneous systems due to certain specific advantages of using solid surfaces [7]. Clay

minerals constitute one such medium. Clay minerals occur abundantly in nature and their high surface area, sorptive and ion-exchange properties have been exploited for catalytic applications through decades. Solid clay catalysts [8, 9] have a broad range of functions including (a) use as catalytically active agents (solid acids) (b) as bifunctional or inert supports (c) as fillers to give solid catalysts with required physical properties.

The layered structure of clays is suitable for the modification by transition metals and subsequent use in catalysis. Grafting of metals on the surface of the clay made it suitable for anchoring various ligands allows chiral and achiral catalysis.

1.1.2 Clay minerals

Clay minerals are the most important chemical weathering product of the soil. They are formed by the alteration of existing minerals or by synthesis from elements when minerals weather to their elemental form. In general the term clay implies a natural earthy, fine –grained material, which develops plasticity when mixed with a limited amount of water. Clays and clay minerals occur under a fairly limited range of geologic conditions. The environments of formation include soil horizons, continental and marine sediments, geothermal fields, volcanic deposits, and weathering rock formations. Most clay minerals are formed when rocks come into contact with water, air or steam. Extensive alteration of rock to clay minerals can produce relatively pure clay deposits that are of economic interest.

Clay minerals are distinguished from other colloidal materials by the highly aniometric and often irregular particle shape, the broad particle size distribution, the flexibility of the layers, the different types of charges, the heterogeneity of the layer charges, the pronounced cation exchange capacity, the disarticulation (in smectites) and the different modes of aggregation.

Chemically, clays are microcrystalline, hydrous aluminium (occasionally Mg and/or Fe) silicates. Majority of these minerals have layered structures and therefore are called phyllosilicates, but some have chain structures and these are called inosilicates.

1.2 Structure of Clays

The term clay generally refers to aluminosilicates where the particle size is in the micron range and which exhibit cation exchange capacity. This definition encompasses zeolites, but the term is normally used in connection with sheet silicates only. The atomic structure of clay minerals consists of Al $(OH)_3$ and $Mg(OH)_2$ brucite octahedral unit, both of which form sheet or layer structure(Fig.1.1).

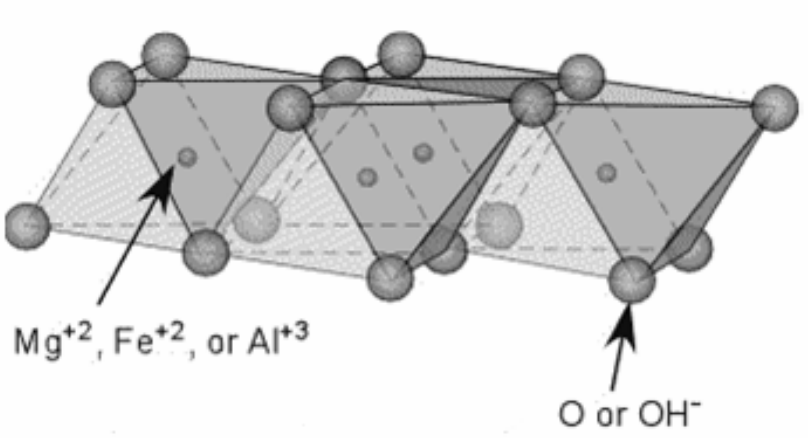


Fig.1.1 Sheet structure of Clay minerals

Tetrahedral layers consist of continuous sheets of silica tetrahedra linked via three corners to form a hexagonal mesh and the fourth corner of each tetrahedron (normal to the plane of the sheet) is shared with octahedral in the adjacent layers. Octahedral layers in clay mineral, on the other hand consists of flat layers of edge-sharing octahedral, each formally containing cations at its center(usually Al^{3+} or Mg^{2+}) and OH^- and O^{2-} at its apices(Fig1.2).

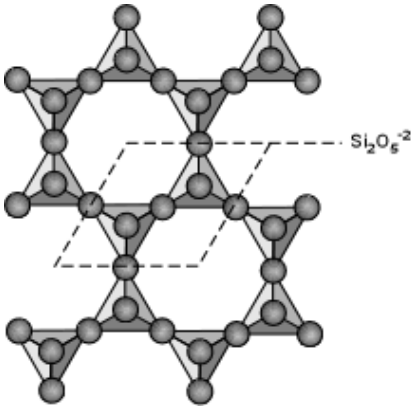


Fig.1.2 Basic structural unit of sheet silicates

Clay is formed by the combination of Sheets of octahedral and tetrahedral units (fig 1.3). The apical oxygen of the tetrahedral layers replaces 2/3 of the hydroxyls in one plane of the octahedral layers. The remaining OH^- ions in this layer are in the centers of the hexagons formed by the oxygens of the tetrahedral layers.

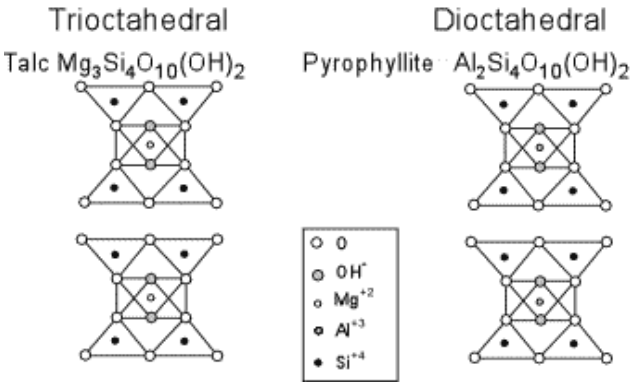


Fig.1.3 Trioctahedral and dioctahedral structure of Pyrophyllite

The different arrangements of tetrahedral and octahedral layers lead to different classes of clay minerals. When trivalent aluminium is the dominant cation in the octahedral layer, only 2/3 of the octahedral sites are occupied. Such a structure is described as "dioctahedral "and there are two octahedral cations per unit cell. When a divalent cation such as Mg^{2+}, is dominant in the octahedral

layer, all the available sites are filled. In this type of structure there are three octahedral cations per unit cell and the structure is described as " trioctahedral".

1.3 Composition of Clays

1.3.1 Kaolinite group

Structure 1:1 dioctahedral

Composition: $Al_2Si_4O_{10}(OH)_8$

The mineral species: Kaolinite[10], narcite[11-12], dickite[13-14], halloysite[15], anauxite[16-18]. Here the charges within the structural unit are balanced. There is a slight substitution of Ti and Fe for Al. Halloysite is the hydrous form of kaolinite. The presence of interlayer water in halloysite makes the bond rather weak. Halloysite occurs in tubes whereas the rest of the minerals in this group are tabular.

1.3.2 Montmorillonite or Smectite group

This group of minerals contain two dioctahedral or trioctahedral layer and one tetrahedral layer.

Composition: $Mx/nYH_2O[Al_{4.0}\text{-}xMgx]Si_8O_{20}(OH)_4$

The mineral species is either a dioctahedral smectites such as montmorillonite, beidellite and nontronite or trioctahedral smectites such as hectorite, saponite, sauconite [19-21] etc. They have a charge deficiency either in the octahedral or tetrahedral layer.

1.3.3 Pyrophyllic Group

Structure: 2:1 dioctahedral

Composition: $Mg_3Si_4O_{10}(OH)_2$

The layers are electrically neutral so that no interlayer cation is present. If aluminium replaces silica, the structure is no more neutral. To balance it K^+ may be added which produces muscovite.

1.3.4 Talc

Structure : 2:1 dioctahedral

Composition : $Al_2Si_4O_{10}(OH)_2$

The bonds are held together with Van der Waals forces so it gives a greasy feeling to talc. Layers are electrically neutral, thus no interlayer cation is present [22].

1.3.5 Mica group

Structure: 2:1 dioctahedral or trioctahedral

Composition: $X_2Y_4\text{-}6Si_6Al_2O_{20}(OH)_4$

(X=K, and or Na, Y=Al and/or Fe and/or Mg)

The mineral species includes dioctahedral micas; muscovite, paragonite, phengite, leucophyllite etc and trioctahedral micas such as biotite, phylogopite, lepiolite, taeniolite etc[23-31]. Most commonly the mineral illite (dioctahedral) is closely related to muscovite though it contains less potassium and more water and shows structural variability. Glauconite may be regarded as an iron rich illite that has larger amount of ferric ion than aluminium in the octahedral layer.

1.3.6 Chlorite

Structure: 2:2 trioctahedral

Composition: $(Mg_{6-y-x}Fe_yAl_xSi_{4-x})O_{10}(OH)_8$

Isomorphous substitutions. There are many mineral names for compositionally distinct members of the group and extensive solid solutions occur by ionic substitution between members.

1.3.7 Serpentine Group

Structure 1:1 trioctahedral

Composition : $Mg_6Si_4O_{10}(OH)_8$

The mineral species: Chrysotile-fibrous, lizardite-platy, antigorite-fibrous.

Various substitutions can be made in this group with tetrahedral Al^{3+}, Si^{4+} and Fe^{3+}, octahedral: Al^{3+}, Mg^{2+}, Fe^{2+}, Co^{2+}, Mn^{2+}, Ni^{2+}, and Cr^{3+}.

1.4 Structural Formula for Clays

The composition of any clay-type could be written relative to the proportion of oxides. For example, composition of Kaolinite is $Al_2O_3SiO_2.2H_2O$, but this is virtually devoid of structural information. It is better to take the unit cell as the basic quantity, and then the above formula can be expressed as $(Si_4)_{IV}(Al)_{VI}O_{10}(OH)_8$. This gives the cation occupancy of the tetrahedral sheet (Subscript IV) and the octahedral sheet (subscript VI). All the 1:1 clay mineral have the same anionic group, $O_{10}(OH)_8$. Similary the anioinic group for all 2:1 mineral is $O_{20}(OH)_4$. The unit cell formulae for dioctahedral 2:1 type is $Si_8)_{IV}(Al)_{VI}O_{20}(OH)_4$. Here out of the six octahedral sites, only four are occupied and is by Al. 2:1 trioctahedral type in which tetrahedral cations are Si^{4+} and octahedral cations are Mg^{2+} have unit cell representation as $(Si_8)(Mg_6)_{VI}O_{20}(OH)_4$. Table 1.1 shows the structural formulae for some dioctahedral and trioctahedral 2:1 phyllosilicates.

Table 1.1 Structural formulae of dioctahedral and trioctahedral 2:1 phyllosilicates

Layers	Trioctahedral	Dioctahedral
Octahedral Only T-O	Brucite, $Mg(OH)_2$ Serpentine group $Mg_3Si_2O_5(OH)_4$	Gibbsite, $Al(OH)_3$ Kaolinite group $Al_2Si_2O_5(OH)_4$
T-O-T	Talc group	Pyrophyllite, smectite group $Al_2Si_4O_{10}(OH)_2$
T-O-T with interlayer Cations (eg.,K^+)	Phlogopite Micas $K(Mg,Fe^{2+})_3(Si_3AlO_{10})(OH)_2$	Muscovite micas, illite Clays $K_2(Al)_2(Si_3AlO_{10})(OH)_2$

1.5 Montmorillonite Clays

Montmorillonite, the most important smectite is composed of units made up of two SiO_2 tetrahedral sheets and one Al_2O_3 octahedral sheets (Fig 1.4). The inter sheet layer include, exchangeable metal ions, neutralizing the net negative charges, which are generated by the partial substitution of Al^{3+} with Mg^{2+} at the octahedral sites. To a lesser extend some tetrahedral sites also might be occupied by ions other than Si^{4+}. These characteristics explain the high cation exchange capacity (CEC) and good swelling properties that provide wide applications.

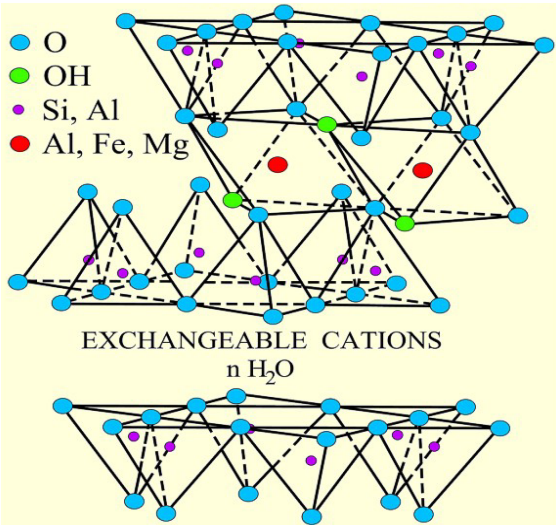


Fig.1.4 Montmorillonite

Calcium is the most common interlayer cation but when sodium is the exchangeable ion, the mineral swells more when placed in contact with water. Replacement of interlayer cation by potassium resembles montmorillonite with illite, but does not lose its ability to take up water. Mineral data of Montmorillonite is given in table 1.2.

Table 1.2 Mineral data of Montmorillonite

Montmorillonite	:	$(Na,Ca)_{0\text{-}3}(Al;Mg)_2Si_4O_{10}(OH)_2.nH_2O$
Crystal Data	:	Monoclinic. Point Group:2/m:Tiny scaly crystals,tabular on {001}; as Lamellar or globular mircrocrystalline aggregates; clayey, compact, massive.
Physical Properties	:	Clevage:{001}, perfect, Fracture: Uneven, Hardness
	:	1-2 D(meas) = 2-3 D(calc,) = n.d. Positive identification of minerals in the Smectite group may need data from DTA curves, dehydration curves, and X-ray Powder patterns before and after treatment by heating with organic liquids.
Optical Properties	:	Translucent, Colour:White, pale, pink, buff, yellow, red, green.
Luster	:	Dull, earthy.
Optical Class	:	Biaxial(-).Pleochroism:X=colourless to pale brown, yellow-Green; Y= dark brown to yellow-green, olive-green, pale yellow; Z=brown To olive-green, pale yellow.
Orientation	:	X~c;Y=b;Z~a. α=1.492-1503, β=1.513-1.534, γ=1.513-1.534 2V(meas.)=10^o-25^o
Cell Data	:	Space group: C2/m. a=5.17(2) b=8.94(2) c=9.95(6) β=n.d Z=1
X-ray Powder pattern	:	Chambers, Arizona, USA; Na and glycerol saturated. 17.6(10),4.49(8), 1.50(6),9.00(5), 3.58(4), 2.57(4b), 2.99(3)
Polymorphism& Series	:	Interstratifies with chlorite, muscovite, illite, cookeite, kaolinite.
Mineral Group	:	Smectite group
Occurrence	:	An alteration product of volcanic tuff and ash, forming bentonite beds, and of pegmatite dikes and wall rocks bordering hydrothermal mineral deposits. Forms under alkaline conditions of poor drainage, with Mg, Ca, Na, and K remaining in the soil.
Chemistry	:	(1) Montmorillonite, France: corresponds to $(Ca_{0.14}Na_{0.02})_{\Sigma=0.16}(Al_{1.68}Mg_{0.36}Fe_{0.04})_{\Sigma=2.08}(Si_{3.90}Al_{0.10})_{\Sigma=4.0}O_{10}(OH)_{2.1.02}H_2O$

	(1)
SiO_2	51.40
$A_{l2}O_3$	19.76
Fe_2O_3	0.83
MgO	3.22
CaO	1.62
Na_2O	0.11
K_2O	0.04
H_2O^+	7.99
H_2O^-	14.81
Total	**99.52**

Association	:	Cristobalite, Zeolites, biotite, quartz, orthoclase, dolomite, amphiboles, pyroxenes, Olivine, calcite, gypsum, pyrite, limonite.
Name	:	After the occurrence at Montmorillonite, France.

1.6 Modification of Clays

Naturally occurring clays may not be efficient catalysts. Shaping the properties such as acidity, porosity, thermal stability, mechanical strength etc of the catalyst can be done with modification of the clay by various methods in order to cope with the need. Various methods of modification include acid activation, cation exchange, intercalation, pillaring, organic modification, chemical grafting etc

1.6.1 Acid activation

One of the most common chemical modifications of the clays, used for both industrial and scientific puroposes is activation by acids. This consists of treatment of clay with mineral acid solution, usually HCl or H_2SO_4. The main task is to obtain partly dissolved material of increased surface area, porosity and surface acidity [32]. From the industrial point of view, the term 'acid-activated clays' was reserved mainly for acid-treated bentonites. Bentonite has always had a multitude of markets and acid-activated bentonite was a traditional product for many decades. It is usually a Ca^{2+}bentonite that was treated with inorganic acids to replace divalent calcium ions with monovalent hydrogen ions and to leach out ferric, ferrous, aluminium and magnesium ions thus altering the layers of smectite and increasing the specific surface area and porosity. This results in the production of bleaching earths, clays suitable for a range of bleaching or decolourising applications, in which they compete against natural bleaching earths [33, 34]. The interest in acid-activated clays as sorbents and catalysts continues because they constitute a widely available, inexpensive solid source of protons which have proven effective in a number of novel and industrially significant reactions and processes. Until their replacement by zeolites in the 1960s acid-activated clays were employed as cracking catalysts [35] and are still currently used in industrial processes such as the alkylation of phenols [36] and the dimerization and polymerization of unsaturated hydrocarbons [37]. Acid-

activated clays have enjoyed renewed interest in their role as high surface area supports for environmentally benign catalysts in Friedel-Crafts alkylation and acylation reactions [38, 39]. The use of these materials include the use of acid-treated clays pillared with oxyhydroxyaluminum species as both catalysts [40,41] and as selective adsorbents for oil clarification [42] and the use of Ti^{IV}-exchanged acid-leached clays as effective Diels-Alder catalysts [43]. As a result of the considerable commercial utilization of acid treated clays for decolorizing oils [44] and in carbonless copying paper [45].

1.6.2 Cation exchange

In swelling clay minerals, such as smectites, the interlayer cations can undergo exchange with cations from external solutions. The concentration of exchangeable cations is called CEC, usually measured in milliequivalents per 100g of dried clay. Since smectites have the highest concentration of interlayer cations, they have the highest cation exchange capacities (typically 70-120 mequiv./100 g). Structural defects at layer edges give rise to additional CEC and a small amount of anion exchange capacity. Clay has an interlamellar water layer containing dissolved cations sandwiched between extended aluminosilicate sheets where two external tetrahedral silica layers surround internal octahedral alumina layer in a tetrahedral octahedral tetrahedral (TOT) structure. By replacing the interlayer ions with high charge density cations like Al^{3+}, $Zn^{2+}$and Fe^{2+} acidity can be imparted in the clay and can be utilized for a broad range of organic transformations [46–48].

1.6.3 Intercalation

Montmorillonite can efficiently adsorb various organic compounds, ionic or neutral, within its interlayers. The intercalation is quite easy accomplished by magnetic stirring of the clay dispersed aqueous solution with an appropriate amount of guest ions dissolved in water or smectites added

directly as a powder. Such intercalation can be utilized as a probe for identification of 2:1 clay minerals [40-50]. Due to ionic exchange with the exchangeable alkali ions, generally, more than 95% of the guest ions are incorporated on the basis of the CEC of the clay [51-52]. Also non ionic guests with large dipolemoments such as ketones and nitriles can be adsorbed to the exchangeable metallic ions within the layers according to their coordination with the ionic sites in the interlayer.

Structural defects at layer edges give rise to additional CEC and small amount of anion exchange capacity. Smectites can be exfoliated into polymer matrices via in-situ polymerization and clay-polymer nano composites exhibit an improvement in the mechanical properties compared with those of the clay alone [53-55], which has attracted increasing interest over last ten years [56, 57].

1.6.4 Pillaring

Eventhough naturally occurring and synthetic clays, which are usually rich in exchangeable Na^+, K^+, or Ca^{2+} cations can be converted into viable acidic catalysts by directly or indirectly inserting protons into the interlamellar regions, such catalysts still suffer from the disadvantage of physical collapse at high temperatures. At 200^{o}C, the interlamellar solvent species (water or a reacting organic layer) tend to collapse, and therefore, sustaining the catalytic activity of the clay at higher temperatures is by inserting pillars, preferably of an inorganic character, which serve to keep the individual layers apart. There is usually a chemical bond between alumino silicate layer and pillar, making this step more or less irreversible. The generation of pillared clays has other advantages, not the least among them being the merit of incorporating extra 'pores'into the catalyst.

Barrer and Mc Leod[58] in 1955 first introduced the concept of transforming a lamellar solid into a porous structure by inserting laterally spaced molecular props between the layers of smectite clay mineral. They used

organic compound, tetraalkylammonium ions to develop porosity. However, organic and organometallic intercalating or pillaring agents decompose at relatively modest temperatures causing the PILC structure to collapse. The terms 'pillared and 'pillaring' originates from the work of Brindley and Semples [59] and Vaughan and Lussier [60] in 1970 on smectite type clay minerals. They found that thermally stable, robust inorganic moieties could be intercalated between the individual clay platelets of the stack or aggregate of Clay lamellae. These materials are referred to as pillared interlayered clays(PILCS). Nowadays, a range of materials that can be pillared has expanded beyond smectite type clay minerals. Metal oxide pillared clays for elements other than Al or Zr are also very useful as cracking catalysts, such those derived from polyoxochromium polymers, obtained from the hydrolysis of Cr (III) hydroxides [61].

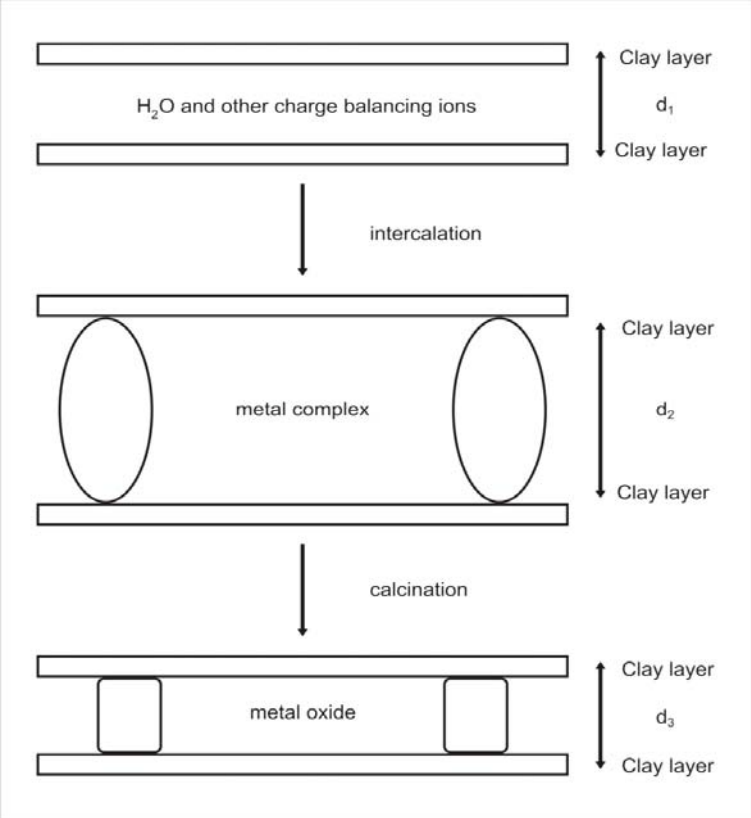


Fig.1.5 Schematic representation of Pillaring.

1.6.5 Organic modifications

In recent years, many materials, resulting from the covalent grafting of organic units on inorganic surfaces, have been developed, mainly for chromatographic applications [62]. The covalent grafting of organic units on an inorganic surface leads to materials combining functionalities and specific properties of the support [63]. These functionalized inorganic solids have a potential as "integlligent materials"[64].

However, reports in the literature of such covalent grafting on natural minerals, aluminosilicates particularly, are rather scarce. Choudiri et.al have reported the anchoring of palladium (II)catalysts [64-66] and of onium salts[67] in the interlamellar spaces of montmorillonite. Alberti et.al[68] reported the synthesis of organically-modified zirconium phosphate with uniform pore size by controlling the ordering of organic units[69]. Organosilane reagents have been used to graft organic units on silanol groups of various minerals [70]. An unsuccessful attempt on kaolinite was reported [71]. However, sylanisation of the external surfaces of kaolin clays was achieved [72]. This route involves chloro or alkoxy silanes with reaction presumably involving edge SiOH groups. The treatment of Montmorillonite with trichloro and alkoxy silanes has been reported, resulting in organic loadings of up to 25 wt%, with the intended application of hazardous material remediation [73] and they observed no increase in the clay's basal spacing, suggesting that the organic compounds are bound to the outer clay edges. Methacrylate-terminated alkoxy silanes were also used to treat the edge of laponite for applications in emulsion polymerization [74]. Reactions on the aluminum hydroxyl groups of minerals have been very rarely reported. Inoue et al. have reacted ethylene glycol[75], other glycols, and aminoalcohols[76] on gibbsite to obtain organic derivatives of bohemite. Johnson and Pinnavaia[77,78] have silylated the external AlOH surfaces of a tubular

aluminosilicate, imogolite. Kaolinite is a 1:1 layered aluminosilicate whose aluminum side is made of a gibbsite-type layer, hydrogen bonded to the silicate side of an adjacent layer [79]. This provides kaolinite with a large cohesive energy, which prohibits expansion which is found in the smectite family. However, the Al-OH layer would be a candidate for grafting organic moieties, if access could be provided to the reagent. Intercalation of polar organic molecules, such as dimethyl sulfoxide(DMSO) or N-methyl formamide(NMF) in the interlamellar spaces of kaolinite has been extensively studied[80-84]. A series of organo kaolinite derivatives of DMSO or NMF intercalates of alocols and glycols were reported by Deteller et.al [85]. Diethanolamine(DEOA) and triethanolamine(TEOA) covalently grafted kaolinte has been reported[86].

1.6.6 Composites

Over the past several years, much research was focused on polymer-clay nanocomposites[87]. Most methods till date have focused on exchanging cations in the clay gallaries with long-chain aliphatic quarternary ammonium or phosphonium compounds [88-90]. This substitution increases the clay gallery spacing and creates a more favorable organophilic environment for polymer penetration and interaction. Another route to forming hydrophobic clay uses trialkoxy silanes as the silicon source during clay synthesis [91, 92]. Also Sol-Gel reaction in the presence of dispersed organically modified montmorillonite was used to form delaminated clay structures [93]. All of these clays modified in some form, can then be used in polymer matrix nanocomposites. Two common methods of exfoliating clay in polymer matrix include insitu polymerization and polymer mixing methods by melt compounding or solvent casting [94]. Both generally involve organically surface modified-clay. Free radical grafting of polyacrylamide on to organophilic montmorillonite has been recently reported by Mansoori et al. [95].

1.7 Properties of Clays

1.7.1 Swelling

Many clay minerals absorb water between their layers, which move apart and the clay swells. For efficient swelling, the energy released by cations and/or layer solvation must be sufficient to overcome the attractive forces (such as hydrogen bonding) between the adjacent layers. In 1:1(OT) clay minerals (kaolinite), water forms strong hydrogen bonds with hydroxyl groups on hydrophilic octahedral layers, allowing swelling to occur. With 2:1 (TOT) clay minerals, the ability to swell depends on the solvation of interlayer cations and layer charge. Clays with 2:1 structures and low layer charge (e.g.talc and pyrophyllite) have very low concentration of interlayer cations and therefore do not swell readily. At the other extreme, those with very high layer charges (e.g mica) have strong electrostatic forces holding alternate anionic layers and interlayer cations together, thus preventing swelling. Those with univalent interlayer cations swell most readily and with divalent, trivalent and polyvalent cations, swelling decreases accordingly. The extent of swelling can be observed by measuring interlayer seprations using powder X-ray diffraction.

1.7.2 Acidity

An important source of acidity in clays is the generation of protons from the ionization of water molecules coordinated to the exchangeable cations. This occurs because of the interlamellar space. The proton thus generated attaches itself to a surface oxygen atom. The acidity is therefore crucially dependent upon the nature and concentration of the exchangeable cations. Some of these cations may be protons or polarizing cations (e.g.Al^{3+}) which give rise to strong Bronsted acidity [96]. The higher the electronegativity of M^{+}, the stonger are the acidic sites generated. Bronsted acidity also stems from the terminal hydroxyl groups and forms the bridging oxygen atoms. In addition, clay minerals have layer surface and edge defects, which would result

in weaker Bronsted and/or Lewis acidity, generally at low concentrations. The acid strength is usually expressed by the Hammett scale. On this scale, the acidity of clay minerals can be comparable to that of concentrated sulphuric acid. The surface acidity of natural clays with Na^+ or NH_4^+ as interstitial cations ranges from +1.5 to -3. Washings of the clay with mineral acid, such as HCl, brings down Hammett(H0) function from -6 to -8, which is between Con.HNO_3(-5) and H_2SO_4(-12).

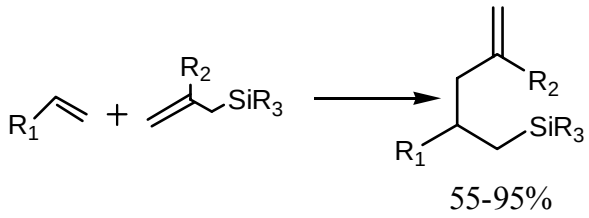
1.8 Clay Catalysis in Organic Synthesis

Clays have a long history of use as catalysts and supports in organic reactions [97]. Several excellent reviews on clay catalysed organic reactions have appeared in the recent past [98-100]. Both in their native state and in numerous modified forms, clays are versatile materials that catalyse a variety of chemical reactions. Just as they can be moulded into any shape, their micro structure can be changed to suit chemist's need to promote diverse chemical reactions. The amazing amenability of clays for modification lies in the fact that the interlamellar cations can be very easily replaced by other cations or other molecules. Molecules can be covalently anchored to layer atoms.

Zhou et.al briefly summarized the emerging trends in synthetic clay based materials[101]. Much of the work on clays focus on the use of "normal" smectites, mostly the commercially available K10 and KSF or native varieties with Bronsted or Lewis acid sites and enhancing their catalytic performance by pillaring techniques to manipulate the pore size, surface area and stability or replace interlayer cations to alter acid-base properties[102-103]. Clays have been intercalated with a variety of inorganic and organic ions, metal complexes and organic compounds. These have brought about radical changes in the performance of clays in terms of increasing the rates of reactions, yields, product selectivity, and stereoselectivity including enantioselectivity [104-107].

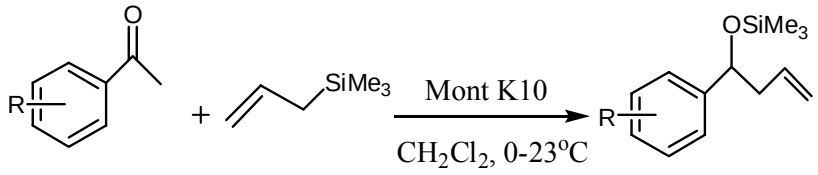
1.8.1 Addition reactions

Several types of addition reactions facilitated by montmorillonite clays have appeared in the literature in the past ten years by various group of workers. They include addition of allylsilanes to C=C and C=O bonds, carbene addition, epoxidation, Michel addition, etc. Motokura et.al [108] have found excellent catalytic performance by proton exchanged montmorillonite in the addition of allylsilanes to aromatic and aliphatic alkenes (Scheme 1).



Scheme 1 Addition of allyl silanes to aliphatic alkenes

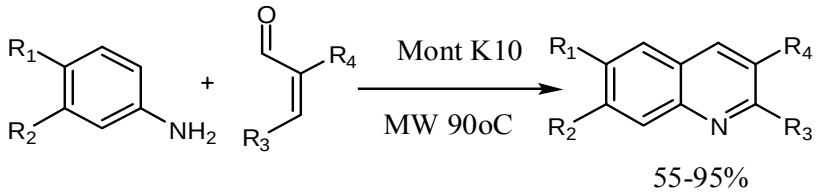
Dintzner et.al reported [109] that activated montmorillonite K10 clay catalyst was found to catalyse the reaction of allyl trimethylsilane with aromatic aldehydes to give homoallyic silyl ethers. This modified Hosomi-Sakurai reaction is environment friendly and delivers protected homoallylic ethers due to six membered pericyclic transition state of ene reaction [scheme 2]. Allylation of ketones and aldehydes has been carried out using potassium salts of allyl and crotyltrifluroborates using boron trifluoride etherate or montmorillonite K10 catalyst [110], the K10 catalysed reactions are better stereoregulated with the diastereomeric ratio being greater than in the case of $BF_3.OEt_2$ catalysed reactions.



R=$2NO_2$, $3NO_2$, 3F, 4Cl etc 70-99%

Scheme 2 Addition of aliphatic trimethyl silanes to aromatic aldehydes

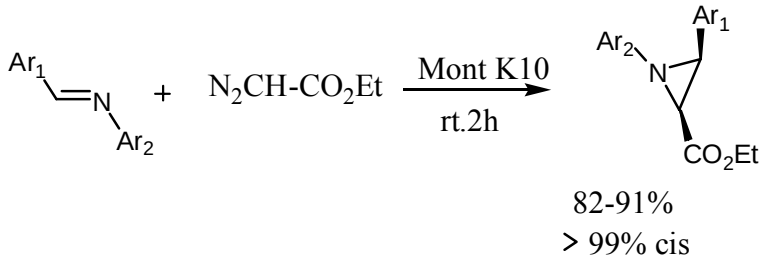
Synthesis of quinolines in good to excellent yields catalysed by Montmorillonite K10 under solvent free condition with the assistance of microwave has been reported [111] (Scheme 3).



R_1 =H, CH_3, C_2H_5, F, Br, Cl
R_2= H, CH_3, Cl
R_3= C_6H_5, 2-NO_2-C_6H_5
R_4=H, CH_3

Scheme 3 Addition of aniline derivatives to cinnamaldehyde

Synthesis of ethers by the addition of alcohols to olefins is an important reaction catalysed by Bronsted acids. The problem, however, in such reactions is the possibility of extensive isomerisation of the double bond through the intermediate carbocation. Wang and Guin[112] reported the selective addition of methanol to 2,3-dimethyl -1-butene catalysed by suphuric acid-treated montmorillonite reducing the possibility of extensive isomerisation of the double bond and the suphuric acid-treated montmorillonite was found to be better than other solid acid catalysts. Triazenes have been synthesized by adding p-aminobenzene-1-sulfonyl azide or amide to a cold mixture of sodium nitrite and acid treated clay (K10, bentonite, or Kaolin), followed by a cyclic secondary amine, which adds to the diazo intermediate formed in the previous steps [113]. Borkin et al. [114] reported the preparation of cis-aziridines in high diastereoselectivity (>90%) and excellent yields(82-91%) by reacting Schiff bases with ethyl diazoacetate in the presence of montmorillonite K10 as catalyst at room temperature for 2h. K10 was the best catalyst among the several other acid catalysts such as $H_4W_{12}SiO_{40}$, Nafion-H, Amberlist-15 and Nafion-H on silicon (Scheme 4).

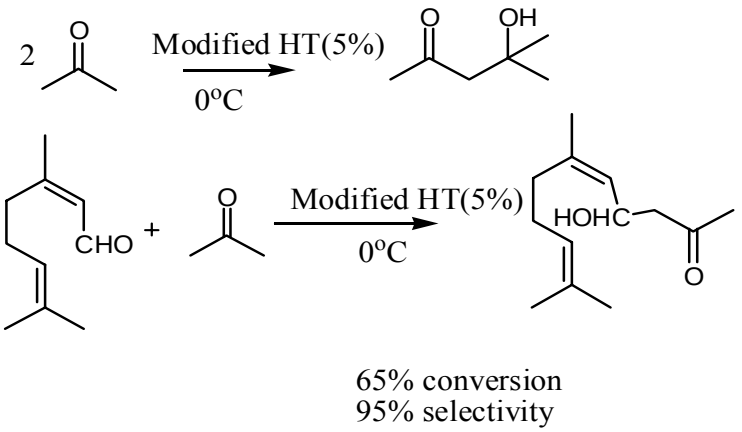


Scheme 4 Synthesis of cis aziridines

1.8.2 Condensation reactions

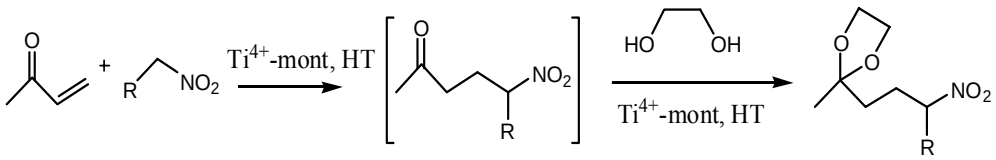
Carbon-Carbon bond forming reactions are of primary importance in organic synthesis, among the numerous procedures developed for this purpose, aldolization/aldol condensation occupies an important position. The aldol reaction is catalyzed by acids as well as bases. A base is the preferred catalyst to obtain aldol. Because of the importance of these reactions much attention is being paid to develop environmental friendly procedures using heterogeneous catalysts.

Hydrotalcites(HT) were found to be active catalysts in the self condensation of acetone and cross condensation of acetone with citral. Modified hydrotalcite catalyst at 0^oC showed high activity and a small amount of catalyst was required (5%) [115]. These reactions are 100% atom economic and are examples for good "green procedures" (Scheme 5).



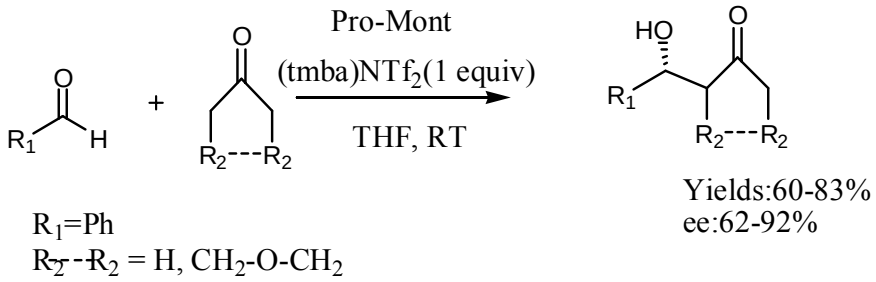
Scheme 5 Aldol condensation of acetone catalysed by modified hectorite

Sequential acid and base catalysed condensation reaction in one pot by acid layered and base layered clay has been reported. Montokura et.al [116] mixed Ti^{4+} intercalated montmorillonite with surface tunable basic hydrotalcites. The acid-base catalyst combination acts sequentially in multistep reactions that require both acid and base catalysis. The authors report the following multi step reactions, (i) deacetalization-aldol condensation, Michael addition-aceatalization (ii) esterification-aldol condensation-epoxidation (iii) esterification-aldol condenation-Michael addition (Scheme 6).



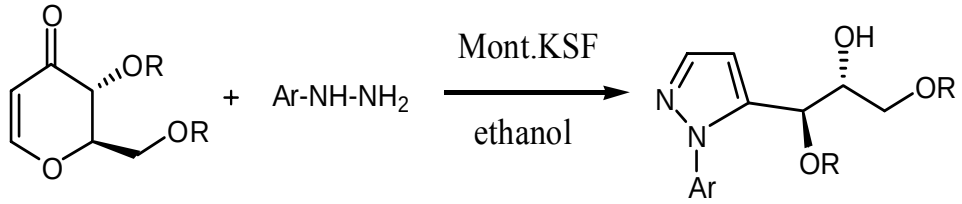
Scheme 6 Sequential acid base condensation by clay catalysts

Knovenagel condensation of malononitrile with carbonyl compounds has been found to be activated by ultrasound and catalysed by alkaline-doped saponites [117]. Mukaiyama crossed aldol condensation of silyl enol ethers with various aldehydes catalysed by montmorillonite K10 [118] was reported. Prolium exchanged montmorillonite acts as chiral molecular catalyst to induce chirality in the newly formed asymmetric carbon of the aldol product [119]. (Scheme 7).



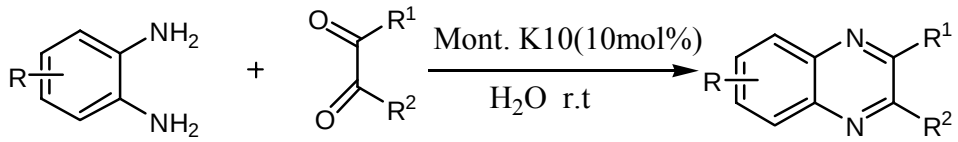
Scheme 7 Enantioselective synthesis of aldols

A three- step reaction of addition of phenylhydrazines to dihydro 4-H-pyranone derivatives, followed by ring opening and intramolecular condensation to deliver pyrazines in good yields is promoted by montmorillonite KSF clay in ethanol solvent. The stereochemistry of the substituent is retained in the products [120] (Scheme 8).



Scheme 8 Pyrazines from dihydropyranones

Montmorillonite K10 catalysed synthesis of quinoxalines by the condensation of 1,2-diketones with o-phenylene diamines in water has been reported[121]. The reaction takes 3h and gives excellent yields (scheme 9).

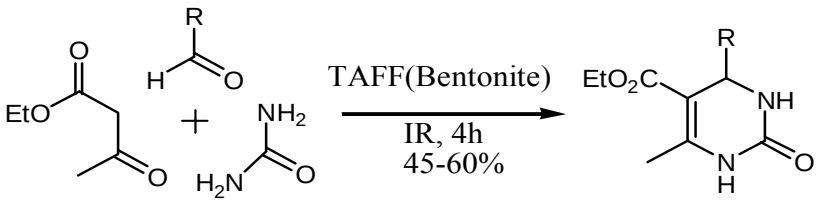


R= H, CH_3, NO_2
R_2= C_6H_5

90-100% when R=H
70%, When R=NO_2

Scheme 9 Montmorillonite catalysed synthesis of quinoxalines

Salmon et al.[122] have shown that one pot condensation of β-ketoesters/ β-dicarbonyl compounds with aldehydes and ureas catalysed by bentonite clay TAFF under infrared irradiation in the absence of solvent gives dihydropyrimidinones (Scheme 10).



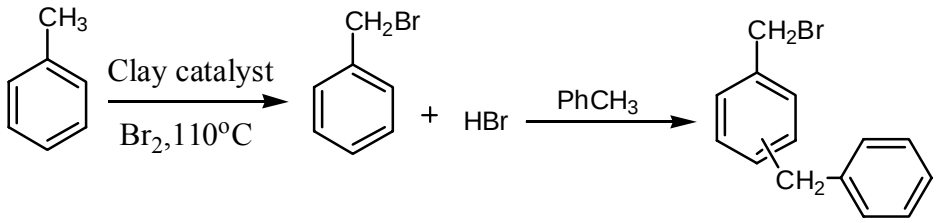
R= CH_3, C_6H_5,
X= O,S

Scheme 10 Solvent free Biginelli reaction

1.8.3 Friedel crafts and related reactions

There are numerous disadvantages in using stoichiometric amounts of aluminium chloride in the industrially significant Friedel-Crafts reaction that are associated with pollution load on the enivironment. Montmorillonite supported transition metal salts(zinc and nickel chlorides) are highly active and selective reagents for the catalysis of Friedel-Crafts alkylation.

It is an electrophilic substitution reaction of usually aromatic and hetero aromatic compounds by alkyl or acyl groups catalysed by a number of Lewis and Bronsted acids under homogeneous and heterogeneous conditions. Alkyl halides, alcohols, sulfonates and olefins are used for acylation. Industrially important benzyl toluenes have been synthesized by clay-catalysed benzylation of toluene through bromination[123]. Using commercially available montmorillonite K10 and bentonite catalysts, the products have been obtained in good yields in a continuous process. During the reaction HBr formed is recycled and re-oxidised to bromine by air (Scheme 11).

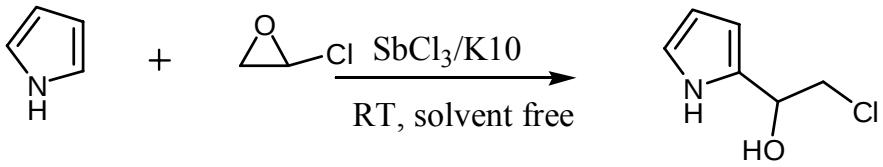


Scheme 11 Preparation of benzyl toluene

Ga/AlClx-grafted montmorillonite-K10 was found to be an efficient catalyst for benzylation as well as benzoylation of benzene, substituted benzenes and naphthalene, using benzyl chloride and benzoyl chloride respectively[124] (Scheme 12).

Scheme 12 Benzylation reaction

Montmorillonte-supported cupric nitrate has been used in the regioselective nitration of aromatic hydrocarbons [125]. A vastly increased para-preference is reported in the nitration of halobenzenes [126]. Lieu et al [127] have prepared an efficient montmorillonite K10 supported antimony trichloride catalyst for alkylation of nitrogen heterocycles, pyrrole, indole and indole derivatives, using epoxides as alkylating agents. The reaction occurs at room temperature under solvent free condition in a short period of time in good to excellent yields (Scheme 13).

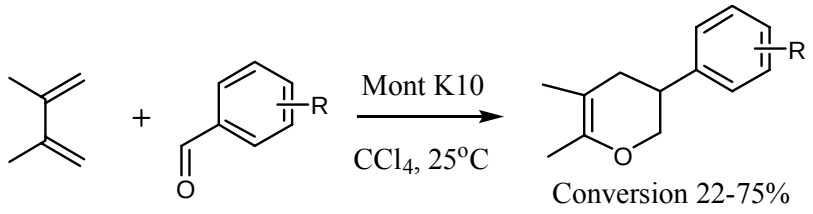


Scheme 13 Alkylation of nitrogen heterocycles by epoxides

1.8.4 Diels Alder reactions

The Diels-Alder reaction is a cycloaddition process between a 4-electron and a 2-electron component which could be starting compounds or intermediates formed in a multistep reaction sequence. Many such reactions are assisted by acid catalysts. This has provided an opportunity to exploit clays, particularly montmorillonites, as Bronsted and Lewis acid catalysts for

Diels alder reaction. Fe(III)-doped K 10-montmorillonite, in combination with 4-tert-butylphenol, is a potent catalytic system for unactivated dienophiles in the Diels-Alder reactions[128]. Dintzner et al.[129] found that the carbonyl group of benzaldehyde and its derivatives add to 2,3-dimethyl-1,3-butadiene under the influence of montmorillonite K10 clay in CCl_4 at 25°C to form dihydropyrans (Scheme 14).



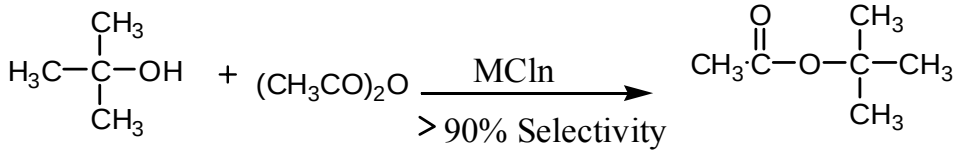
R= H, o-OMe, o-OEt, o-F, o-Cl

Scheme 14 Hetero Diels Alder reaction of benzaldehyde with dimethyl butadiene

1.8.5 Esterification reaction

Esters are naturally occurring alkyl or aryl carboxylates, which have found numerous applications in various industries. Several methods are available for the synthesis of esters such as i) Reaction of alcohols or phenols with carboxylic acids, carboxylic acid anhydrides or acyl halides ii) addition of carboxylic acids to olefins iii) addition of alcohols to ketenes etc. The most common method is the acid catalysed reaction of an acid with alcohol, H_2SO_4 is the common acid used in this process. This has many disadvantages such handling, corrosion etc. Replacement of H_2SO_4 with Clay catalyst circumvents most of these problems.

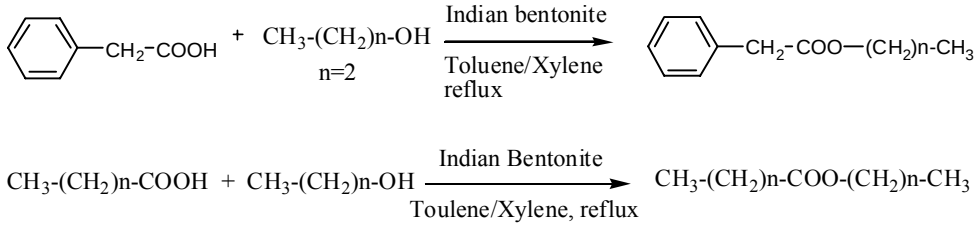
Kaolin, Montmorillonite K10 and KSF supported with transition metal chlorides, $InCl_3$, $GaCl_3$, $FeCl_3$ and $ZnCl_2$ were employed to esterify tert-butanol with acetic anhydride to tert-butyl acetate with more than 98% selectivity [130]. The K10 Clay was found to be the best support and $InCl_3$ was the best catalyst (Scheme 15).



Scheme 15 Esterification of tert-butanol with acetic anhydride

Wallis et al[131] have employed the esterification of maleic anhydride with p-cresol, along with a transacetalisation reaction, diacetylation of benzaldehyde with acetic anhydride and tetrahydropyranylation of ethanol to improve the catalytic activity of different batches of commercially available montmorillonite K10 clay. Thermally activated Nigerian ukpor kaolinite clay and Udi clay were shown to be good catalyst for the preparation of n-propyl acetate [132].

Ferric chloride supported K10 was found to be an efficient esterification catalyst [133]. Vijayakumar et al. [134,135] have shown that acid activated Indian bentonite was a good catalyst, in some cases better than zeolites for the preparation of aryl and alkyl esters (Scheme 16).

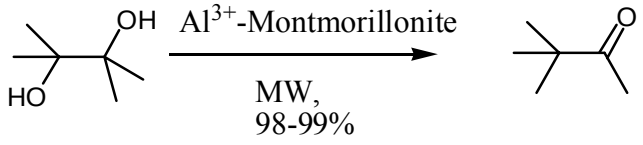


Scheme 16 Esterification of aryl and aliphatic acids with Indian bentonite

1.8.6 Rearrangement reactions

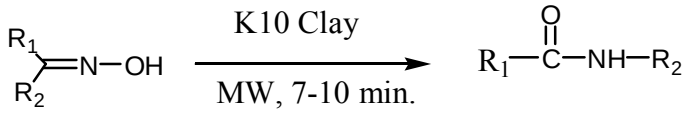
Rearrangement or isomerisation reactions are important in producing large number of fine chemicals. A majority of such transformations are brought about by conventional Lewis and Bronsted acid-catalysts. A variety of acid calys effectively catalyse such reactions. Al^{3+}-montmorillonite K10 effectively catalyses the rearrangement of gem-diols to give product in

excellent yield [136]. The comparison of this method with conventional oil bath heating protocols revealed that the reaction times are too long for the conventional method (Scheme 17).



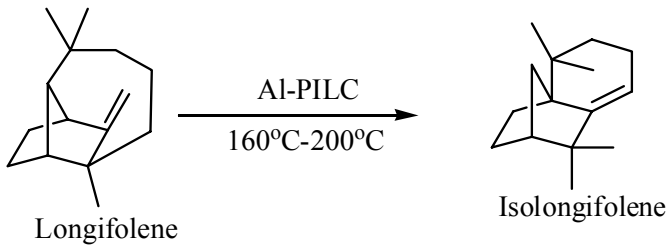
Scheme 17 Rearrangement of gem-diols

Montmorillonite K10 clay in dry media is reported to give Beckmann rearranged product of ketoxime under dry media in good yields [137] (Scheme 18).



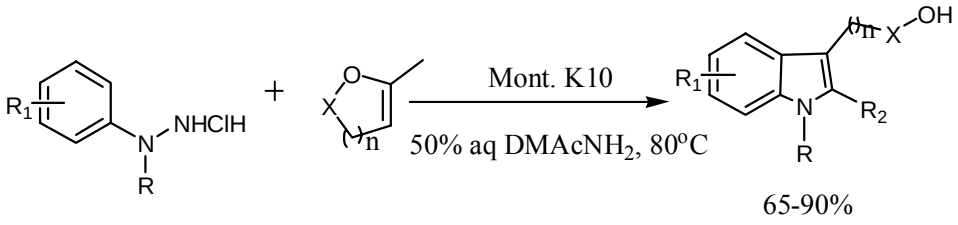
Scheme 18 Beckmann rearrangement of ketoximes

Isolongifolene is a commercially important tricyclic sesquiterpene used extensively in the perfume industry. It is obtained by acid-catalysed isomerisation of longifolene. Singh et al. [138] have used alumina and zirconia pillared clays and Ce^{3+} and La^{3+} modified montmorillonite clays for the conversion of longifolene to isolongifolene. They found that Al^{3+} pillared montmorillonite clay showed the highest conversion and reasonable selectivity (Scheme 19).



Scheme 19 Iomerisation of Longifolene

Montmorillonite K10 catalyses the [1, 3] sigmatropic shift following the addition of aryl hydrazine hydrochlorides to cyclic enol ethers and enol lactones to give a variety of substituted indoles[139](Scheme 20).

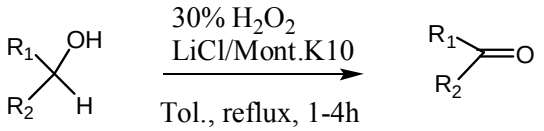


R=Ph-CH_2,R_2 =Me, X=CO
R_1=H, p-Me, p-F, p-Cl
R_2 =H, Me
n=1,2; X=CH_2, CO

Scheme 20 Arylhydrazine addition to cyclic enol ethers and enol lactones to form indoles

1.8.7 Oxidation reaction

The common procedure for the oxidation of alcohols to ketones or aldehydes make use of compounds of transition metals, such as chromium, manganese, vanadium, etc., which are toxic. It is desirable to reduce their use or replace them by oxidants that are less hazardous to health and environment. Many clay-based oxidizing agents that fullfil this Green chemistry condition have been developed. Eftekhari-Sis et al.[140] reported the oxidation of alcohols to aldehydes and ketones using hydrogen peroxide as oxidizing agent in the presence of lithium chloride supported on montmorillonite K10(Scheme 21). Varma, et al. [141] reported a facile microwave assisted oxidation of alcohols to carbonyl compounds using clayfen, under solvent free conditions. Interestingly primary alcohols afforded aldehydes exclusively with no formation of the corresponding carboxylic acids.

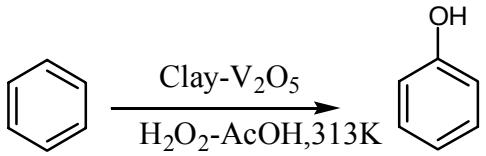


R_1= CH_3-$(CH_2)_5$, $CH_3(CH_2)_2$, C_6H_5-CH_2, $C_6H_5(CH_2)_2$, 2-Cl-C_6H_4

R_2= H, CH_3, C_2H_5, C_6H_5, COOH, C_6H_5-CO

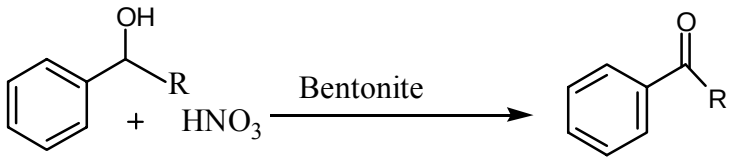
Scheme 21 Oxidation of alcohols with Montmorillonite

The oxidation of benzene to phenol by vanadium oxide catalyst supported on clay(chlorite, illite, and atapulgite from Inner Mongolia) using hydrogen peroxide as co-oxidant was reported recently[142]. The presence of acetic acid enhances the hydrogen peroxide reaction as it avoids phase separation problem (Scheme 22).

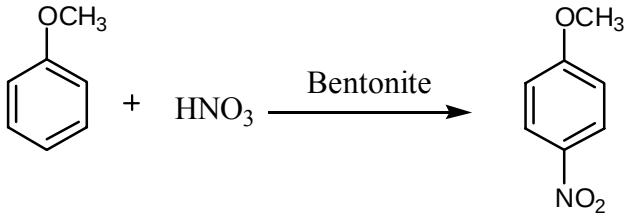


Scheme 22 V_2O_5-on-clay/H_2O_2-AcOH for hydroxylation of benzene to phenol

Nitric acid and metal nitrate salts are used as both oxidizing and nitrating agents depending on the nature of the substrate and reaction conditions. In most cases the reaction is slow, but if vigorous conditions are used to hasten the reaction the substrate may decompose. However, reports show that such reactions can be accomplished under very mild conditions, if the reagents are supported on smectite clays. In the presence of dilute nitric acid natural bentonite oxidizes benzyl alcohol to corresponding carbonyl derivative. In contrast, the same reagent-catalyst system could nitrate activated aromatic compounds regioselectively [143] (Scheme 23).

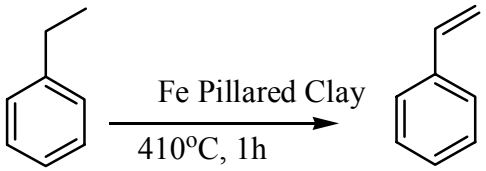


R=H, alkyl



Scheme 23 Substrate-based oxidation or nitration using nitric acid

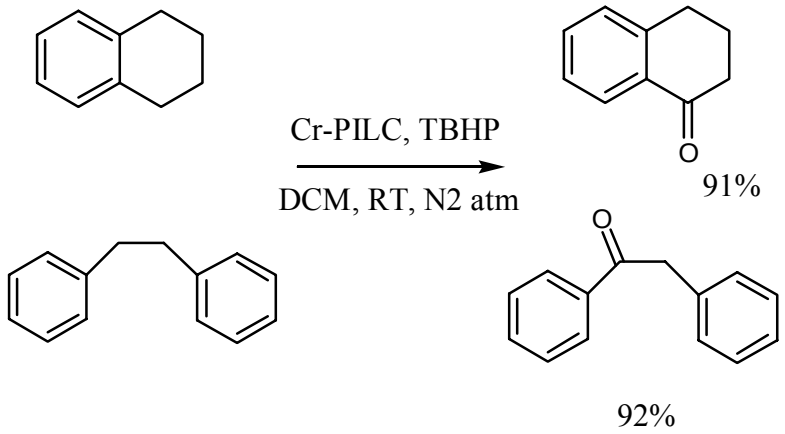
Ethylbenzene has been dehydrogenated to styrene using processed Venezeulan smectite clay intercalated with trinuclear iron complex $[Fe_3O(OAc)_6.3H_2O]^+$. Ethyl benzene was heated over the catalyst for 1h at 410°C. There was 50% increase in styrene formation with the use of this catalyst [144] (Scheme 24).



Scheme 24 Oxidation of ethyl benzene to styrene

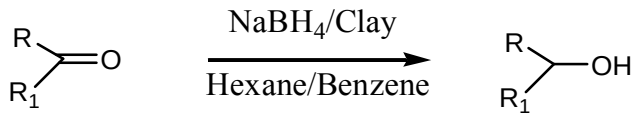
Choudary et al.[145] reported a mild and efficient method for benzylic oxidation of aryl methylenes to the corresponding carbonyl compounds in good yield using a catalytic amount of chromim-pillared montmorillonite and equimolar quantities of tert-butyl hydroperoxide. The method is very selective towards monocarbonyl compounds of the substrates prone to form dicarbonyl compounds. The heterogeneous catalyst is inert toward the branched hydrocarbons and has been put to practice to obtain p-isobutylacetophenone selectively from p-isobutylethylbenzene. Further, the method is extended

successfully to the oxidative debenzylation reactions for the first time. A striking feature of the oxidative deprotection with the present method is the deprotection of a benzyl group from the substrates having an alkyne moiety (Scheme 25).



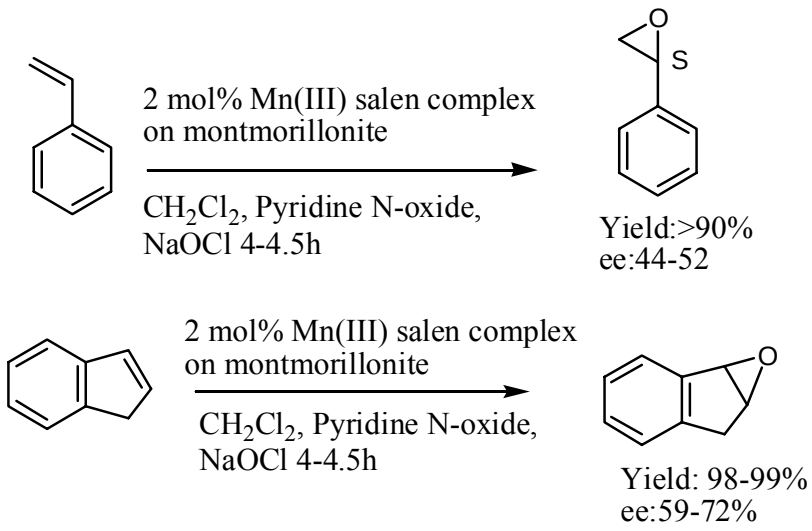
Scheme 25 Benzylic oxidation of aryl methylenes

The selective reduction of carbonyl group of various aromatic and aliphatic compounds bearing different functional groups was accomplished with sodium borohydride in the presence of clay in aprotic solvents to the corresponding alcohols in good to excellent yields [146] (Scheme 26).



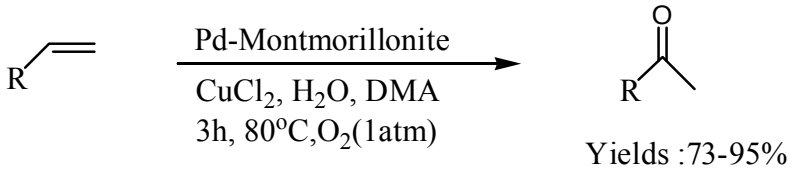
Scheme 26 Reduction of carbonyl group to alcohols using clay

A Mn(III)-salen complex immobilized on montmorillonite in the presence of pyridine N-oxide and sodium perchlorate was used for the enantioselective epoxidation of styrene and indene in high yields(Scheme 27). The enantiomeric excess appeared to be strongly dependent on the structure of the substrate [147].



Scheme 27 Enantioselective epoxidation reactions

Palladium ion-exchanged montmorillonite in the presence of $CuCl_2$, was developed as a highly efficient heterogeneous catalyst for the Wacker oxidation of terminal olefins to the corresponding methyl ketones. The catalyst was resusable and retained its activity and selectivity (Scheme 28) [148].

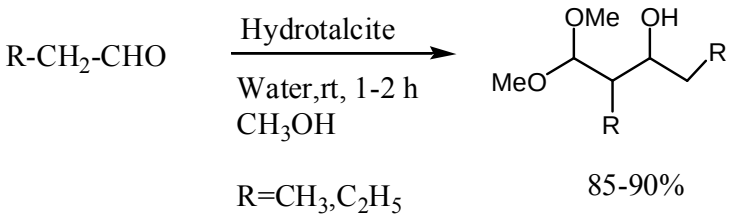


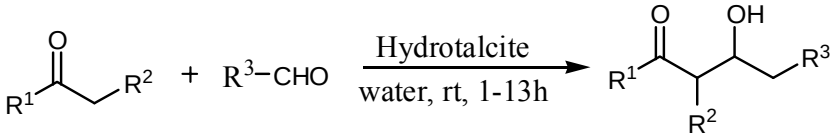
R=C_4H_9,C_6H_{13},$C_{10}H_{21}$,$C_{14}H_{29}$,$C_{18}H_{37}$, Cyclohexyl, etc

Scheme 28 Wacker oxidation of terminal olefins

1.8.8 Base Catalysed Reactions

Reconstructed hydrotalcites efficiently catalyzed the aldol reaction of carbonyl compounds in the presence of water. The catalyst was reusable. In the presence of water, the hydroxyl ions present on the surface of the reconstructed hydrotalcite acted as Bronsted base sites to abstract hydrogen ions from the reactants (Scheme 29) [149].



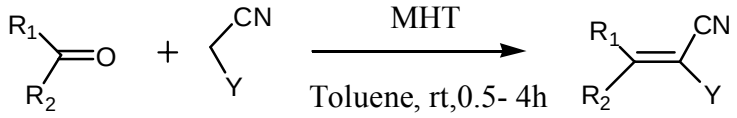


67-78%

R^1= CH_3
R^2 =H
R^1, R^2= Cyclopentyl
R^3 = $(CH_3)_2CHCH_2$,$(CH_3)_2CH$, C_3H_7

Scheme 29 Aldol condensation in the presence of water

The Knovenagel condensation between various carbonyl compounds and malonitrile and ethyl cyanoacetate was efficiently catalysed by a modified Mg-Al hydrotalcite(MHT) catalyst(Scheme 30) [150].



Yields 50-100%

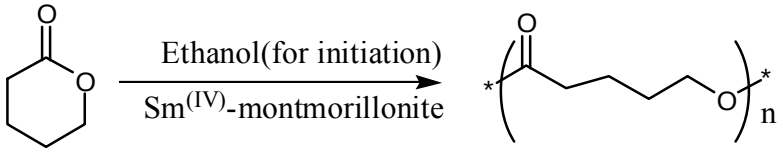
R^1 = C_6H_5, C_6H_5CH=CH, 2-furyl,3-furyl, 2-CH_3O-C_6H_4
R^2 = H, CH_3
R^3 = CN, CO_2Et

Scheme 30 Knovenagel condensation

1.8.8.1 Ring opening and ring closure reactions

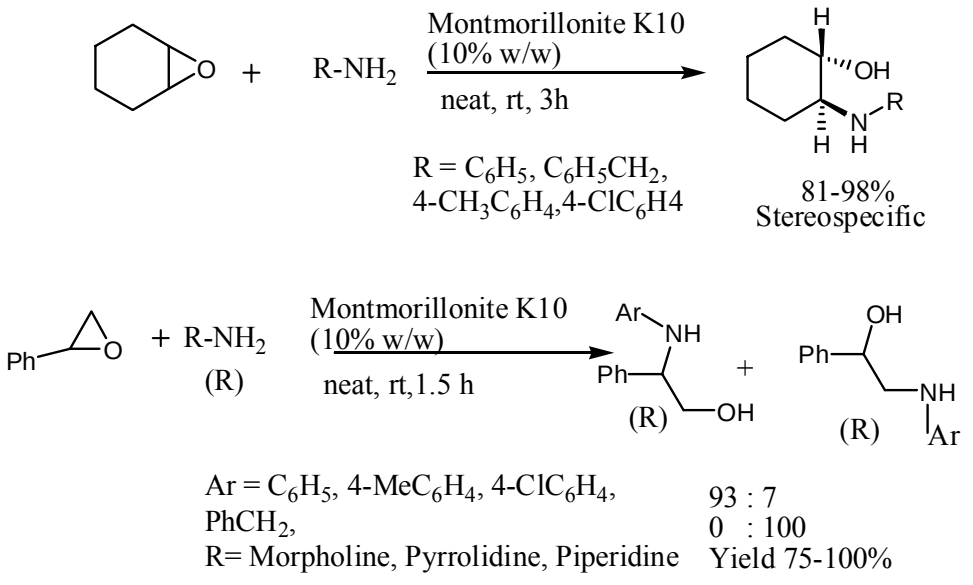
Ring-opening polymerization of δ-valerolactone to polymeric products with controlled molecular weights was catalysed by tin(IV) ion-exchanged montmorillonite in a solvent free system, although a minute amount of ethanol

was used to initiate the reaction. The aluminium (III)- and iron (III) exchanged montmorillonites were also effective for the polymerization of δ-valerolactone (Scheme 31) [151].



Scheme 31 Ring opening reaction of δ-valerolactone

The ring opening of epoxides by amines were carried out efficiently in the presence of montmorillonite K10 providing amino alcohols with excellent regio and stereoselectivity. The regioselectivity for unsymmeterical epoxides was controlled by electronic and steric factors associated with the epoxides and the amines. It provides an improved and efficient method for the preparation of β-aminoalcohols(Scheme 32)[152].



Scheme 32 Ring opening reactions of epoxides

Over the past three decades, clay catalysts became mainstream solid acid of choice for organic synthesis. The clay minerals with their inherent Lewis and Bronsted acid sites can catalyse a number of organic reactions with a great number of advantages as compared to conventional acids. The properties of these minerals can be modified with different metal cations, or organic /organometallic compounds easily to suit the need of an organic chemist to assist a particular type of reaction thus providing exceptional importance for these materials in the development of new synthetic processes. The inexpensive and environmentally friendly nature of these solid acids led to their wide use in research laboratories. The chemists are keen on reducing the pollution and developing greener reaction conditions such as use of solid acid catalyst, use of water as solvent etc. In this point of view, clays are suitable candidates in terms of cost, accessibility and handling. The developments in modification and application of clay minerals are still continuing in various organic processes as their acidity is much higher than that of zeolites, and their mechanical properties (durability, surface area etc.) are much better than that of acidic ion exchange resins, they are considered as the envrionmenatally benign acid catalysts of the future.

1.9 Main Objectives of the Present Work

The main objectives of the present work are

- To prepare clay supported Titanium catalysts based on K10 Montmorillonite and Montmorillonite KSF using titanocene dichloride as titanium source. Physico-chemical characterization of the prepared catalysts using UV-DRS, FT-IR, EDX, BET surface area and pore volume measurements, XRD, SEM and TG/DTA studies. Application of these catalysts for the synthesis of tetrasubstituted imidazoles and Mannich bases, optimization of reaction parameters. Characterisation of the products by FT-IR, ^{1}H NMR spectral studies.

- To prepare aluminium pillared saponite. Physico-chemical characterization of the catalyst by IR, TG-DTA, AES, XRD, Surface area and pore volume measurements. Application of this catalyst for the synthesis of acetals of pentaerithritol and optimization of reaction parameters.
- To prepare Cu-Pd, Co-Pd exchanged bimetallic clay catalysts by simple ion exchange method, the physico-chemical characterization of the catalyst and application of these catalysts in Heck-Coupling reactions.
- To prepare Chiral dipeptide metal complex supported Montmorillonite K10 catalyst, their characterization and application in Aza-Diels Alder reaction.
- To prepare a few heteocyclics by conventional and microwave assisted conditions using clay catalysts. Comparison of conventional and microwave conditions.

1.10 Materials and Methods

The aim of active research in catalysis is to produce and reproduce a commercial product, which can be used as stable, active and selective catalyst. Changes in the preparation conditions can result in dramatic alteration in the properties of the final catalyst. In spite of numerous studies, preparation of heterogeneous catalysts is still regarded as an art, often kept secret by the producer. Many synthetic routes have been furnished so as to achieve a sufficient surface area, good porosity, suitable mechanical strength and activity for a particular organic reaction.

A thorough characterization of the prepared catalyst systems was undertaken using different spectroscopic as well as quantitative methods. A

brief discussion of the characterization methods adopted along with the experimental aspects is given in the following sections.

1.10.1 Energy dispersive X-ray spectroscopy (EDX)

Energy Dispersive X-ray spectroscopy (EDX) is a promising and widely used technique for elemental analysis. Use of this technique was accelerated since 1960s as a result of the development of solid-state detectors, nuclear electronics and small computers. An electron beam of energy typically in the range of 10-20keV strikes the surface of a conducting sample. This causes X-rays to be emitted. The interaction of X-rays with an object causes secondary (fluorescent) X-rays to be generated, which can be detected and displayed as a spectrum of intensity against energy. Each element present in the object produces X-rays with different energies. The positions of the peaks are used identify which elements are present and peak heights are used to indentify how much of each element is present. Thus qualitative as well as quantitative elemental mapping is possible. The advantages of electron microscopic analysis over conventional wet chemical analysis are

- X-ray sampling is non-destructive
- Natural heterogeneity is retained
- Analysis can be conducted on microgram quantities
- Adjacent structures can be directly compared
- Excellent probe size(20 to 200 nm)

EDX is accurate and fast and the effort for sample preparation is minimal. If conditions are optimized minimum detection limits can be below the nanogram level for small laboratory instruments and into the femtogram region for more advanced instrumentation. The disadvantages of the instrument are; it is not sensitive to measure low concentrations such as trace elements (those present at a level below about 0.1%). Again, it is not responsive to elements lighter than sodium.

EDX analysis of the catalyst samples prepared was done using a JEOL Model JED – 2300 instrument. Samples were prepared by dusting the clay powder onto double sided carbon tape, mounted on a metal stub (SAIF, STIC CUSAT).

1.10.2 X-Ray Diffraction

X-ray diffraction (XRD) by solids is the most widely employed method for the determination of three dimensional structures of solid substances. XRD is applied to derive information on the fine structure of materials- crystallite size, lattice strain, chemical composition, state of ordering etc. In a material an infinite number of lattice planes with different miller indices exist and each set of plane will have a particular separation dhkl. In clays the interlayer spacing is of the d100 plane [153].

From the Braggs equation,

$$n\lambda=2d\sin\theta$$

d_{100} spacing is determined which is a measure of the distance between the clay layers upon modification for catalytic applications.

In powder XRD, there will be all possible orientation of the crystal. Each lattice spacing will give rise to a cone of diffraction. Each cone consists of a set of closely spaced data each one of which represents a diffraction pattern of a single crystallite within the powder sample. Detector used in powder XRD is sensitive to X-rays. Scanning of the detector around the sample along the circumference of a circle cuts through the diffraction cones at various diffraction maxima. The intensity of X-rays detected as a function of detector angle 2θ is obtained.

The X-ray diffraction pattern of the powdered clays are obtained by using a Rigaku D MAX III VC Ni-filtered Cu K alpha radiaton (λ= 1.5404A^o at a scan rate 4^o/min) (SAIF, STIC CUSAT).

1.10.3 Surface area analysis

Brunauer, Emmett and Teller developed the most common method of measuring surface area [154]. The concept of this method is an extension of Langmuir theory which could be extended to multilayer adsorption. The heat of adsorption of all layers except the first layer is equal to the liquefaction of the adsorbed gas. Summation over an infinite number of adsorbed layers gives the final expression as follows

$$P/V(Po-P)=1/VmC + (C-1)P/VmC\ Po$$

Where

V = Volume of gas adsorbed at pressure P,

Vm = Volume of gas adsorbed in monolayer, same unit as V

Po = Saturation pressure of adsorbate gas at the experimental temperature

C = a constant related exponentially to the heats of adsorption and liquefaction of gas

$$C = e(q1-qL)/RT$$

Where

qL = heat of liquefaction of adsorbed gas on all other layers

R = The gas constant

A graph of P/V (Po-P) Vs P/Po gives a straight line, the slope and intercept of which can be used to evaluate Vm and C

The surface area of the catalyst can be calculated from Vm, if the average area occupied by an adsorbed molecule is known.

$$S.A=VmNoAm/22414W$$

Where N^o is the Avogadro number, A_m is the molecular cross sectional area of adsorbate and W is the weight of the sample. Adsorption of N_2 gas at its boiling point is generally used for surface area measurements using BET

method. t-plot method is used for the determination of microporous surface area, in this method, the adsorbed N_2 volume is plotted against statistical thickness(t) of adsorbed N_2 layer to yield micropore volume on the basis of

$$V = Vmicro+10^{-4}S_ot$$

Where Vmicro is the volume of N_2 adsorbed in micropores and S_o is the external surface area. A universal t-curve of N_2 has been established which gives,

$$t = [13.99/0.034\text{-}\log (P/Po))]^{0.05}$$

Where t is in A^o. If the plot of V versus t gives a straight line passing through the origin, the test solid is considered to be free of micropores.

The surface area and pore volume of the catalyst samples was measured on a Micromeritics Gemini 2360 surface area analyser. Previously activated samples were degassed at 300^{o}C und N_2 for 3h and then brought to N_2 boiling point.

1.10.4 Fourier Transform Infrared (FTIR) Spectroscopy

Infrared absorption spectroscopy is a rapid non destructive and economical physical method universally applicable for structural analysis. The IR spectrum of clay mineral is sensitive to its environmental changes upon modifications such as isomorphous substitution, pillaring and preparation of clay supported catalysts. A number of research works has been carried out on the quantitative clay mineral analysis using infrared spectroscopy. Vibrational spectroscopic investigations yield useful information about hydration characteristics, interlayer cations and moisture content in clays. The FTIR spectroscopy applied to clay mineralogy lies in its ability to characterize the functional group and fingerprint region of very small quantities of samples [155]. FTIR spectroscopy can be used for studying intermolecular bonding

features like distortion of molecular units at various lattice sites, the structure of molecular units in solids, the coordination polyhedra of metal ions, etc. The vibrations of the OH are sensitive indicators of their environment in the clay matrix. The absorption coefficients of the OH stretching vibration bands are assumed to be constant within dioctahedral[156-159] or trioctahedral clay minerals[160-161]. The absorbance of each OH band is proportional to the number of absorbing centers of each type. When all the OH vibration bands occurring in the FTIR spectra are correctly assigned, the FTIR spectra can be quantitatively used [162]. The OH vibrations are affected by the octahedral cations to which the OH groups is coordinated, and to a lesser extent, by the tetrahedral and interlayer environments [163-167].

FT-IR spectra of clay samples were recorded by the KBr pellet method on a JASCO FT-IR spectrometer in the range 400-4000cm^{-1}.

1.10.5 Thermogravimetry (TG)

Thermal stability of the prepared catalyst can be studied by thermogravimetric analysis. It finds wide applications in the determination of different parameters on the preparation of the catalyst, nature and composition of active phase, effect of added promoters or presence of impurities on the catalyst, dispersion of active phase and active phase support interactions, nature and heterogeneity of active sites on catalyst surface, nature of different bound states of adsorbates on catalyst surface, mechanistic aspects of the reaction under investigation, transient chemical changes that occur on the surface, catalyst deactivation and regeneration. Briefly, the method consists of heating a small amount of the substance at a constant rate up to 1000^{o}C or as close to fusion as is possible experimentally, and recording, by suitable devices, the endothermic and exothermic effects that take place in the material. The temperature at which the thermal effects takes place and their intensities are different for many minerals.

TG analysis of the dried samples was performed on a Perkin Elmer Pyris Diamond 6 thermogravimetric/differential thermal analyzer by heating the sample at a rate of $10^{o}C\ min^{-1}$ from room temperature to $800^{o}C$ in N_2.

1.10.6 Ultraviolet Diffuse Reflectance Spectroscopy (UV-DRS)

The technique is used for recording the UV spectrum of solid samples although it can be used for the study of liquids or paste like materials also. Since only the surface of the sample is responsible for reflection and absorption of incident radiation, it is used in the chemistry and physics of surfaces. In situ identification and determination of a variety of substances is possible.

The most appropriate theory treating diffuse reflection and transmission of light scattering layers is the general theory developed by Kubelka and Munk. For infinitely thick, opaque layer the Kubelka-Munk equation can be written as

$$F(R\alpha)=(1-R\alpha)2/2R\alpha=k/s$$

Where Rα is the diffuse reflectance of the layer relative to a non absorbing standard such as MgO, K is molar absorption coefficient of the sample and s is scattering coefficient. Provided 's' remains constant, a linear should be observed between F(Rα) and K[2].

In catalysis the information regarding the interaction between the support and active phase, chemical changes upon modification of the catalyst system can be understood. Metal centered (d-d) transitions and charge transfer transitions can be clearly differentiated by UV-DRS.

UV-DRS spectra of samples were recorded using a Varian Cary 5000 in the range of 175-3300nm (SAIF, STIC CUSAT).

1.10.7 Scanning Electron Microscopy (SEM)

The Scanning Electron Microscope (SEM) is uniquely suited for studying clays because it affords a magnified, three-dimensional view of the unmodified (natural) clay surface with great depth of focus. Compositional analysis of a material may also be obtained by monitoring secondary X-rays produced by the electron-specimen interaction [168]. Scanning Electron Microscopy examines the structure by bombarding the specimen with a scanning beam of electrons and collecting slow moving secondary electrons that the specimen generates. The electron beam and the cathode ray tube scan synchronously so that an image of the specimen surface is formed. The samples are coated with a thin film of gold to make it conducting to prevent surface charging and to protect the material from thermal damage by electron beam.

The main drawback of this technique is that the scan results may not represent the entire sample.

The SEM pictures were taken on a JOEL Model JSM-6390LV(SAIF, STIC CUSAT).

1.10.8 Elemental analysis (ICP-AES)

The elemental analysis of the modified clays is done using inductively coupled plasma-atomic emission spectrometer.

Clay samples for analysis are prepared after removing silica. A known weight (W_1) of the sample is taken in a beaker, treated with concentrated sulphuric acid (95%, 30ml) and is heated until SO_3 fumes are evolved. It is cooled, diluted with water and filtered with ash less filter paper. Filtrate is collected; the residue is heated in a platinum crucible and is weighed (W2). To the weighed sample, 40% HF is added in drops, warmed and strongly heated to

dryness. This is repeated 5-6 times, until no fumes of H_2SiF_6 are evolved. It is again incinerated to 800°C for 1h, cooled and weighed (W_3). From the loss in weight the amount of silica present can be estimated using the equation

$$\%SiO_2 = (W_3-W_2) \times 100/W_1$$

The filtrate is diluted to a known volume and a small portion is taken for quantitative ICP-AES analysis.

AES analysis of the samples were recorded by Thermo Electron IRIS INTREPID II XSP DUO at SAIF, STIC, CUSAT

1.10.9 Pyridine adsorption studies

The clay surface contains both Lewis acid and Bronsted acid sites. The strength of Lewis acidity and Bronsted acidity depends on the number of sites. Using Infrared (IR) and Raman spectroscopy, the acidity of solid catalysts can be studied using basic probe molecules [169, 170]. The hydroxyl groups present in the solid catalysts can be identified by IR spectroscopy; consequently the probe molecule interaction can be easily monitored and measured, there by indirectly measuring the Bronsted acidity of the catalyst. The concentration of the hydroxyl groups, and therefore the concentration of potential Bronsted acid sites, could be obtained from the intensity of the corresponding IR band. Different types of O-H groups present on the surface were identified by different O-H stretching frequencies of hydroxyl groups [171, 172] with limited success in most of the cases. Many studies reveal that pyridine molecule is able to simultaneously determine the concentration of Bronsted and Lewis acid sites [173-175]. Acid strength distribution can be estimated when IR is combined with desorption. The characteristic bands of pyridine protonated by Bronsted acid sites (pyridinium ions) appear at 1540 and 1640cm^{-1}, the bands of pyridine coordinated to Lewis acid sites appear at

1450 and 1620cm^{-1}, from the intensity of the corresponding band it is possible to calculate the number of Bronsted and Lewis acid sites.

After treating the clay with pyridine, the samples were heated at 120^{o}C and FT-IR spectra were directly recorded in the region 1650 and 1350cm^{-1}. The data obtained can be directly correlated to the qualitative and quantitative estimation of both Lewis and Bronsted acid sites.

FT-IR spectra of clay samples were recorded by the KBr pellet method on a JASCO FT-IR spectrometer in the range 400-4000cm^{-1}.

1.10.10 High Performance Liquid Chromatography (HPLC)

HPLC is a chromatographic technique used to purify, quantify individual component from a mixture. HPLC utilizes different types of stationary phases, a pump that moves the mobile phase and analyte through the column and a detector provides a characteristic retention time for the analyte. The detector also provides additional information related to the analyte, (i.e.UV-Vis spectroscopic data for analyte). Analyte retention time varies depending on the strength of its interactions with the stationary phase, the ratio/composition of the solvent(s) used, and the flow rate of the mobile phase. It is a form of liquid chromatography that utilizes smaller column size, smaller media inside the column, and higher mobile phase pressures. With HPLC, a pump (rather than gravity) provides the higher pressure required to move the mobile phase and analyte through the densely packed column. The increased density arises from smaller particle sizes. This allows for a better separation on columns of shorter length when compared to ordinary column chromatography.

Enantiomers of products were found using HPLC Schimadzu, using chiral column CHIRALPAK AD.

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Chapter 2

PREPARATION, CHARACTERIZATION AND APPLICATIONS OF CLAY SUPPORTED TITANIUM CATALYSTS

Contents

The activity of a catalyst in a particular organic reaction is influenced by the method of preparation and pretreatment conditions. Titanium containing clay catalysts were prepared by modification of montmorillonite clays. Physicochemical characterization of the prepared catalyst was done by techniques like EDX, surface area anlaysis and pore volume measurements, XRD, FT-IR, TG, UV-DRS and SEM. The acidity of the catalyst was studied by pyridine adsorbed FT-IR spectra of pyridine adsorbed. Conducting organic reactions under solvent free conditions and use of solid acid catalysts are important points of concern in terms of green chemistry. Solvent free synthesis of tetra substituted imidazoles and Mannich reaction are studied in detail. Substitution effects of the substituted imidazoles were studied theoretically by designing isodesmic reaction conditions.

2.1 Introduction

Montmorillonite, a clay mineral formed by the weathering of volcanic ash, may have played a central role in the evolution of life. Because of its

structure, montmorillonite tends to adsorb organic compounds and this contributes to its ability to catalyze a variety of organic reactions. It is shown experimentally that RNA molecules bind efficiently to clays and that montmorillonite can catalyse the formation of longer molecules (oligomers), thus lending support to RNA hypothesis. This theory proposes that life based on RNA proceeded to current life, which is based on DNA and protein [1]. Montmorillonite clays, a class of inexpensive and noncorrosive solid acids, have been used as efficient catalysts for a variety of organic reactions [2]. The reactions catalyzed by montmorillonite clays are usually carried out under mild conditions with high yields and high selectivities and the workup of these reactions is very simple; only filtration to remove the catalyst and evaporation of the solvent are required. Montmorillonite clays are easily recovered and reused.

2.1.1 Clay supported catalysts

Transition metal ions can be incorporated into the clay matrix to get catalysts for various organic reactions. A series of transition metal ions (Cr, Mn, Fe, Co, Ni, Cu and Zn) loaded on different clays (laponite and montmorillonite) are reported to find use in the synthesis of carbon nanotubes [3]. $GaCl_3$ and $InCl_3$ supported on montmorillonite K10 effectively catalyse the benzylation of benzene by benzyl chloride, the clay supported catalysts were found to be more active than zeolite supported catalysts [4]. Choudhary et al [5], reported that, clay (kaolin, mont-K10 and mont-KSF) supported $InCl_3$, $GaCl_3$, $FeCl_3$ and $ZnCl_2$ catalysts showed high selectivity ($\geq$ 98%) at high conversion in the esterification of tert-butanol by acetic anhydride to tert-butyl acetate and very low activity for the dehydration of tert-butanol at $\leq$ 50°C. Among these catalysts, the montrmorillonite was the best support for esterification reaction. The effect of impregnation of $ZnCl_2$, $MnCl_2$, $FeCl_3$, $SnCl_2$ and $AlCl_3$ on kaolinite and a comparison of natural and activated clay showed that the process led to

catalysts with improved activity, the maximum being associated with $FeCl_3$ when employed in the Friedel- Crafts alkylation of benzene with benzyl chloride [6]. Fe^{3+} ion supported montmorillonite catalyst effectively catalysed the reductive N-acylation of nitroarenes to anilides in moderate to good yield in the presenc of carboxylic acid anhydride [7].

In this chapter, Preparation, characterization and catalytic application of clay supported Titanium catalysts are described in detail.

2.2 Results and Discussion

2.2.1 Preparation of clay supported titanium catalyst

Titanium supported montmorillonite K10 and montmorillonite KSF catalysts were prepared by stirring the activated clay with titanocene dichloride under N_2 atm. The resulting slurry was washed, dried and calcined at 500^oC for 8h. Na^+, Co^{3+}, Cu^{2+} exchanged montmorillonite K10 and Montmorillonite KSF were prepared by stirring the corresponding metal salts with clay overnight, filtered and washed, extensively with water until the filtrate was free from anions. The catalysts were dried at 200^oC for 2h.

2.2.2 Screening of the catalyst

For the synthesis of tetrasubstituted imidazoles and Mannich reaction Montmorillonite K10 clay supported Titanium gave the best result. A detailed study of the reactions including some theoretical studies is discussed in the following sections.

2.2.3 Characterization of clay supported Ti catalyst

The UV-DRS spectra of the parent Montmorillonite K10, and Ti modified catalyst are shown in Fig 2.1, UV-DRS Spectra of Ti/Si catalysts are characterized by broad absorption band centered around 220 nm, 260-270 nm and above 330nm, as reported by Zhang et.al.[8]. Band at.~.230 nm in Ti/Clay

catalysts is associated with isolated Ti (IV) sites, shoulder at 270 nm is probably due to partially polymerized hexacoordinate Ti species. The parent Montmorillonite K10 shows no absorption band in this region.

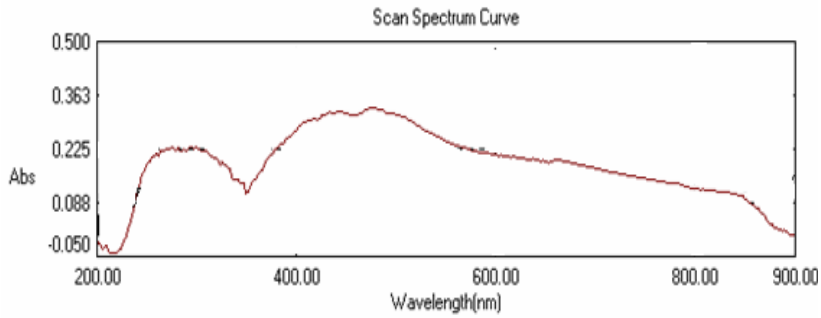


Fig. 2.1 UV-DRS spectra of K10Ti

FT-IR spectra (Fig 2.2) of the parent montmorillonite catalyst show a large band at 3620 cm^{-1}, typical of smectites with large amount of Al in the octahedral sites [9]. Intensity of this peak decreases upon incorporation of Ti in the frame work. This may be due to the formation of Si-O-Ti-OH. IR spectra in the finger print region are characterized by absorptions at 1200-1000 cm^{-1} due to asymmetric stretching and bending vibrations of apical oxygens of SiO_2 tetrahedra and the large band due to combined stretching and bending vibrations of the Si-O bonds are related to basal oxygens [10]. The band corresponding to the Si-O-Si around 1010 cm^{-1} was broadened upon incorporation of Ti in the framework. This may be due to merging of band corresponding to the formation of Si-O-Ti observed around 970 cm^{-1}[8]. Composition of octahedral sheets can be understood from the band around 900 cm^{-1}. Echo bending of Si-O vibrations are observed at 526-471cm^{-1}. Thus the framework vibrations are maintained in both modified and parent catalyst which implies that the basic clay structure was maintained upon incorporation of titanium in the frame work.

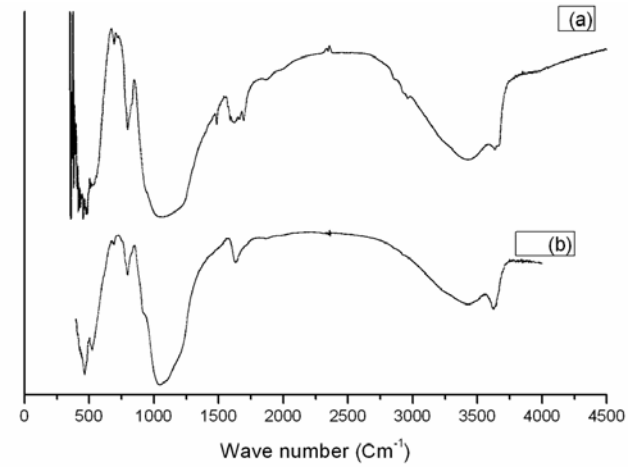


Fig.2.2 FT-IR spectra of a) K10Ti b) K10

The textural characterization of the catalyst was done by studying adsorption isotherm at a temperature lower than or equal to critical temperature. N_2 (77.2 K) is traditionally used as adsorbate. As gas pressure increases, the adsorption proceeds by pore filling of micropores. The potential energy fields from neighboring surfaces overlap and the total interaction energy with adsorbate molecules becomes substantially enhanced giving rise to high gas volume adsorption at very low relative pressures. The surface area and pore volume of the modified clay samples were obtained by applying BET equation. In the present study BET surface area of various catalyst systems are tabulated in Table 2. 1

Table 2.1 Textural properties of various catalyst systems

Samples	SBET(m^2/g)	Pore volume(cm^3/g)
K10Ti	185.3	0.307
KSF Ti	26.8	0.058
Pillared Saponite	169	0.163
K10Cu	233.2	0.414
K10PdCo	155.1	0.183
K10Na	182.2	-----
K10	230	0.36
KSF	15	0.005
KSF Co	72.24	0.117

Montmorillonite K10 has a BET surface area of 230 m^2g^{-1}. In the case of pillared saponite the surface area and pore volume of the catalysts increased drastically. In the case of K10 clay supported transition metal catalysts a decrease or increase in surface area and pore volume is observed depending upon the nature of the metal ion. The surface area and pore volume of K10Ti exhibits a lower value than the parent Montmorillonite K10, which supports the fact of successful incorporation of Ti in the frame work. This is also supported by the relatively low initial adsorption isotherm plot (Fig 2.3).

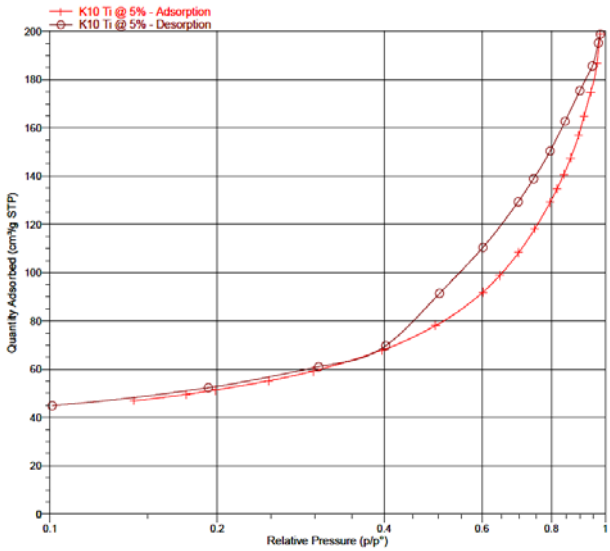


Fig.2.3 N_2 adsorption isotherm of the K10 supported Ti catalyst

The thermal stability of the prepared catalyst systems were studied using thermogravimetric anlaysis. The catalysts were subjected to thermogravimetric analysis in the temperature range 50-800°C using a linear temperature programme at a heating rate of 10°C/min. The TG/DTA profiles of K10Ti (Fig 2.4) shows an endothermic peak corresponding to the loss of physically adsorbed water in the region 80-150°C. The weight loss between 200-250°C may be due to the loss of hydrated water and organic molecules adsorbed on the surface.

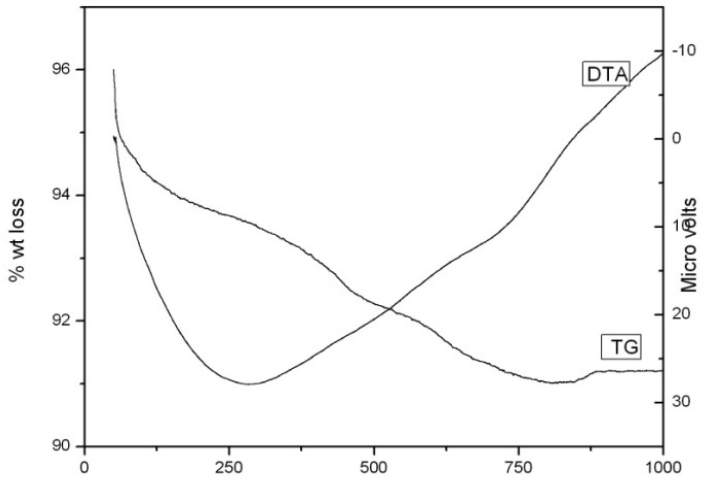


Fig.2.4 TG/DTA of K10Ti

XRD pattern of the parent Montmorillonite K10 and Montmorillonite K10Ti are shown in Fig 2.5. The XRD of K10Ti is identical to that of the parent sample. Thus it can be concluded that the insertion of metal ions in the framework does not destabilize the porous network. Lack of additional peak upon incorporation of metal ions may be due to the diminutive (1-3%) of the exchanged metal ions.

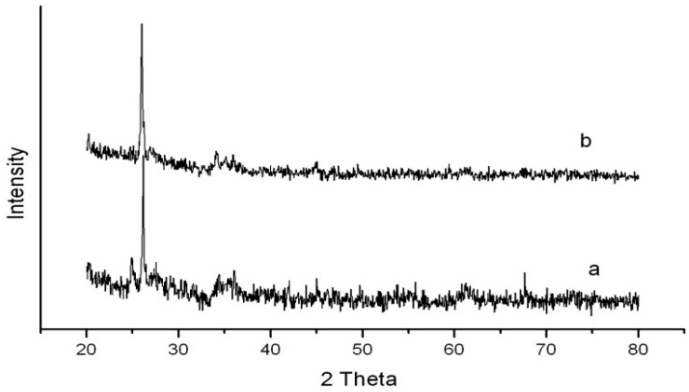


Fig. 2.5 XRD pattern of a) K10 b) K10Ti

The SEM photograph of K10Ti is shown in Fig 2.6. The photograph reveals that the crystalline nature of the clay is maintained and the Ti metal is uniformly distributed. The presence of Titanium in the clay matrix is confirmed by EDX spectra. The results of EDX show that the K10Ti sample contains 0.35% by mass of Ti. (Table 2.2).

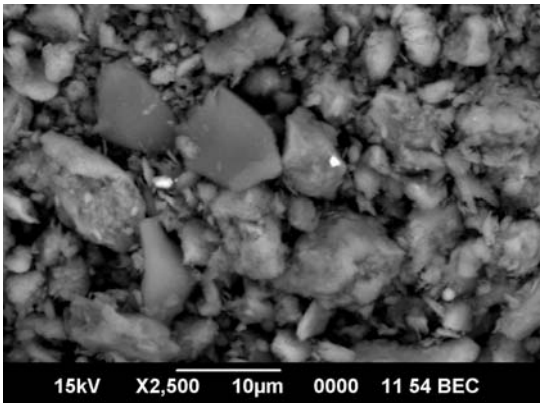


Fig.2.6 SEM image of K10Ti

Table 2.2 Elemental composition of K10Ti by EDX

Element	(keV)	Mass%	Atom%	K
O K	0.525	61.24	73.93	64.79
Mg K	1.253	1.62	1.29	0.809
Al K	1.486	9.06	6.49	5.349
Si K	1.739	22.91	15.76	14.45
S K	2.307	2.29	1.38	1.676
K K	3.312	0.98	0.49	0.813
Ti K	4.508	0.35	0.14	0.261
Fe K	6.398	1.54	0.53	1.179
Total		**100**	**100**	

The metal content of the catalyst was also determined by ICP-AES. The results are shown in table 2.3. The concentration of other elements showed considerable decrease upon modification.

Table 2.3 Elemental analysis of catalysts

	Na	Mg	Al	Ca	Si	K	Fe	Ti
K10	2.18	2.81	17.64	5.01	56.47	4.11	11.6	0
K10Ti	1.7	2.56	14.76	3.64	57.63	3.82	10.16	3.38

2.2.4 Acidity of the catalyst

Clay contains both Lewis and Bronsted acid sites; the total acidity of the clay catalyst is the contribution from both. The acidity of the modified clay catalyst depends upon the acidity of parent clay, metal incorporated and the method used for the modification etc. Lewis acid sites are contributed by metal oxides and Bronsted acid sites are contributed from the structural OH groups which are accessible to probe molecules and which are removed upon heating [11]. The number of Bronsted acid sites decreases with increase in temperature and these sites are practically lost at temperatures above 500^{o}C. Protons from different sources may be the origin of acidity in clays.

The acidity of K10Ti catalyst has been characterized by pyridine adsorption method. The adsorption of pyridine on the surface of clay catalyst is one of the most frequently used methods for the determination of surface acidity. The use of IR spectroscopy to detect adsorbed pyridine enables us to distinguish different acid sites. IR spectra of pyridine adsorbed samples are given in Fig 2.7. The presence of a band around 1450 cm^{-1} is indicative of Lewis acid sites, band around 1490 cm^{-1} may be attributed to pyridine associated with both Lewis and Bronsted acid sites[12,13]. A weak band around 1540 cm^{-1} is indicative of Bronsted acid sites. Intensity of the band can be correlated to the number of acid sites present. In this catalyst, the contribution of Bronsted acid site is more as compared to Lewis acid sites. Thus the total acidity of the present catalyst is the contribution from both. It is shown in earlier reports that Bronsted acid sites in the vicinity of Lewis acidic metal center (active sites) act as co catalyst [14, 15].

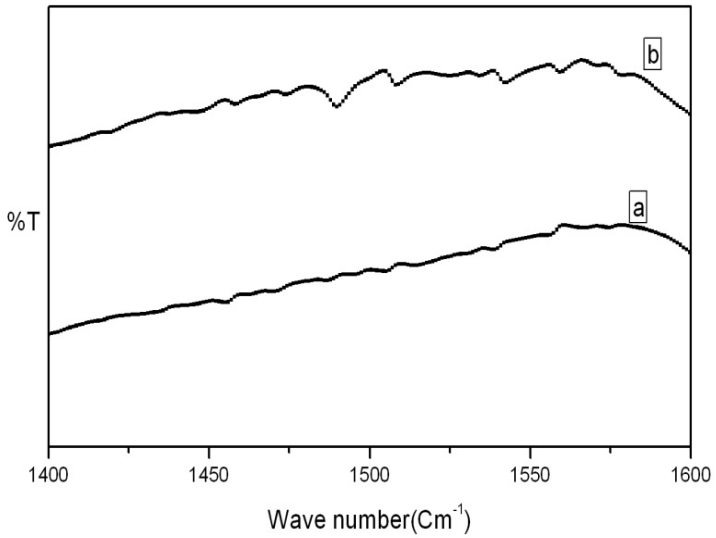


Fig. 2.7 FT-IR spectra of pyridine adsorbed samples a) K10Ti b) Pyridine adsorbed K10Ti

2.2.5 Synthesis of Tetrasubstituted Imidazoles

Imidazoles are important class of compounds for pharmaceutical industry [16]. The imidazole pharmacophore is of therapeutic interest due to its hydrogen bond donor-acceptor capability [17]. Triaryl imidazoles are used as photosensitive materials in photography [18]. In addition, they are of interest because of their herbicidal [19], analgesic [20], fungicidal [21], anti-inflammatory [22], anti-allergic activities [23]. They act as ligands in metallo enzymes and non natural metal complexes [24]. They are components of a number of highly significant biomolecules [25]. The imidazole moiety as a part of the side chain in histidine plays a major role in the biological functions of proteins and peptides. Imidazoles can be synthesized by condensation of benzoin or benzoin acetate with aldehydes, primary amines and ammonia in the presence of copper acetate [26], hetero-Cope rearrangement with aldehyde, ammonium acetate and benzil [27], four component condensations of aryl glyoxals, primary amines, carboxylic acids and isocyanides on Wang resin [28] etc. Synthesis of highly substituted imidazole rings cannot be carried out

in neutral conditions [29]. Use of conventional acids imposes many disadvantages such as handling, corrosion etc. In the classical approach, for the synthesis of tetrasubstituted imidazoles, cyclo condensations proceed with low yields after many hours in refluxing AcOH [30]. Keggin type heteropoly acids as solid acid catalysts were recently reported for the synthesis of tetrasubstituted imidazoles [31]. Karimi et.al reported the synthesis of tetrasubstituted imidazoles under solvent free conditions using various heteropoly acid catalysts [32]. In recent years, considerable interest has been devoted to finding a new methodology for the synthesis of highly substituted imidazoles under solvent-free conditions [33, 34]. The toxicity and volatile nature of many organic solvents, particularly chlorinated hydrocarbons that are widely used in large amounts for organic reactions have posed a serious threat to the environment [35, 36]. Design of solvent free condition and use of water as solvent are the active area of research in green chemistry [37, 38]. Substituted imidazoles are also synthesized by using ionic liquids [39, 40]. N-heterocyclic carbenes are generated from substituted imidazoles [41-45].

However search for new reusable catalysts, which are environmentally friendly, is still continuing. Clays are suitable candidates for this purpose. Due to the presence of layered structure, clays are capable of accommodating ligands [46], the metal ions present in the clays can be exchanged with transition metal ions [47]. Clays can be modified with transition metal ions which show Lewis acidity in the range of H_2SO_4 and HNO_3 and satisfies the above mentioned conditions. Here, we report K10 supported Titanium as a potential catalyst for the synthesis of tetrasubstituted imidazoles under solvent free conditions.

2.2.5.1 Screening of the catalyst for tetrasubstituted imidazole synthesis

Screening of the catalyst for tetrasubstituted imidazole synthesis was carried by reacting, benzil, aldehyde, amine, ammonium acetate and catalyst.

The reaction mixture was stirred at 120°C for 24h; the crude products were separated by extraction using ethyl acetate followed by filtration and purified. The results are summarised in table 2.4. The best result was obtained for K10Ti and was selected for the solvent free synthesis of tetrasubstituted imidazoles.

Table 2.4 Synthesis of tetrasubstituted imidazoles using various clay catalysts

Samples	Time(h)	Yield (%) [a]
K10Ti	2	78
KSF Ti	2	46
Pillared Saponite	2	59
K10Cu	2	65
K10	2	58
KSF	2	30
KSFCo	2	34

Mole ratio. Amine: Benzaldehyde: Benzil: Ammonium acetate is 1:1:1:1
[a] Yields refer to isolated pure products

2.2.5.2 Synthesis of tetrasubstituted imidazoles by K10Ti

2.2.5.2.1 *Optimization of Temperature*

Optimization of temperature of the reaction was carried out by reacting benzil, benzaldehyde, aniline, ammonium acetate in the ratio 1:1:1:1 and catalyst K10Ti catalyst. The reaction mixture was stirred at different temperatures ranging from 80-120°C for 2h; the crude products were separated by extraction using ethyl acetate followed by filtration. It was observed that the yield was increased with increase in temperature up to 120°C and further increase in temperature gave a tarry material. The optimum temperature for the reaction was taken as 120°C.

The results are summarized in table 2.5.

Table 2.5 Synthesis of tetrasubstituted imidazole in the presence of K10Ti supported catalysts under solvent free condition at different temperatures.

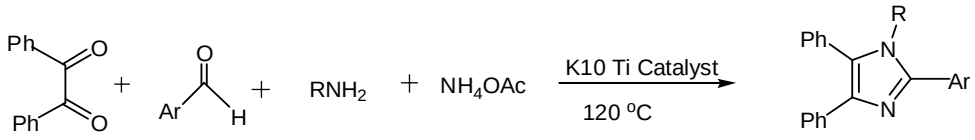
Entry	Temperature (^{0}C)	Time (h)	Yield (%)[(a)]
1	80	2	59
2	90	2	62
3	100	2	68
4	120	2	78

[a] Yield refers to isolated pure products

2.2.5.2.2 *Effect of catalyst loading*

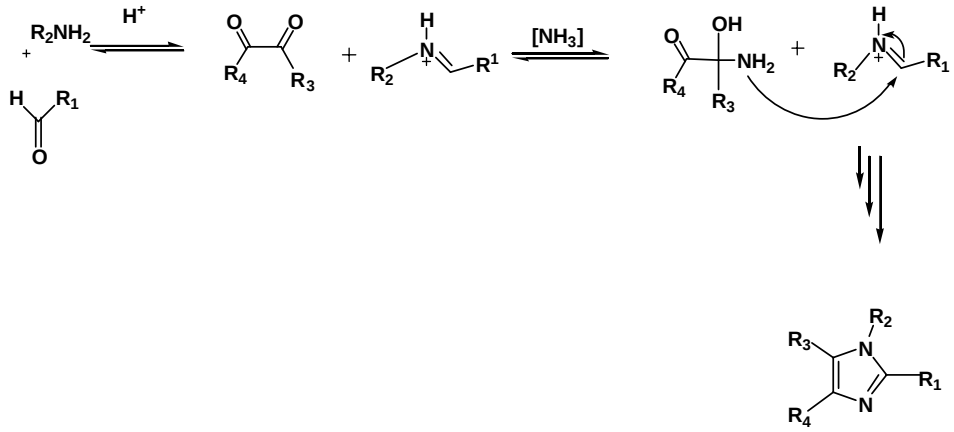
Amount of catalyst was optimized by maintaining the temperature at 120^{o}C, the substrates were taken in the same mole ratio as mentioned above. The catalyst concentration was varied from 50 mg to 250 mg. Up to 250 mg there was an increase in the yield of the product, further increase in concentration has no effect on the yield, and the optimal catalyst concentration was taken as 250 mg.

The solvent free synthesis of tetrasubstituted imidazoles was carried out at optimized conditions i.e temperature 120^{o}C and 250 mg of K10Ti as catalyst. The general scheme of the reaction is given in Scheme 1.



Scheme 1 Synthesis of tetrasubstituted imidazoles

2.2.5.2.3 *Mechanism of formation of tetrasubstituted imidazoles*



Scheme 2 Proposed Mechanism of the reaction

One possible mechanism for the reaction is proposed. The primary amine reacts with an aldehyde to form an imine; diketone upon abstraction of ammonia gets converted to aldamine. Aldamine and imine upon electron rearrangement gave the corresponding imidazole. The role of the catalyst is to enhance the rate of formation of imine in the first step. This is supported by the results discussed in the forth coming page.

In view of the current emphasis on solid state synthesis and on "green chemistry" we set out to develop a solvent free method for the preparation of imidazoles using non poluting catalyst. Benzil, ammonium acetate, benzyl amine, and benzaldehyde were selected as substrates in a model reaction. The model reaction in the absence of catalyst showed no yield after 24 h at 120 ^{o}C and low yield was obtained with unmodified K10. This reaction took place with 0.25 g of different supported catalysts in neat conditions by heating at 120^{o}C. The efficiency of the catalysts to promote this heterocyclization reaction was correlated to the strong acidity of the supported catalysts. The generality and scope of the reaction is summarized in Table 2.6. It can be observed that the process tolerates both electron

donating and electron withdrawing substituents on the aldehyde. It was found that, the reaction proceeded efficiently in all cases, even for nitrobenzaldehyde (entry 11)

Table 2.6 Solvent free synthesis of tetrasubstituted imidazoles using modified K10Ti catalyst

Sl No.	R^1	R^2	Time (h)	Yield % [a]
1	C_6H_5	C_6H_5	2	78
2	4-ClC_6H_4	C_6H_5	2	80
3	4-NO_2-C_6H_4	C_6H_5	2	81
4	C_6H_5	$C_6H_5CH_2$	3	84
5	C_6H_5	CH_3	4	68
6	4-ClC_6H_4	CH_3	3.5	65
7	4-$NO_2C_6H_4$	CH_3	2.5	76
8	C_6H_5	4-BrC_6H_4	3.5	74
9	C_5H_3S	C_6H_5	3	69
10	C_6H_5	C_2H_5	4	72
11	3-NO_2 C_6H_4	C_2H_5	2.5	74
12	4-Cl C_6H_4	C_2H_5	3	73
13	C_5H_3S	CH_3	3	72
14	4-$CH_3C_6H_4$	C_2H_5	3	78
15	4-Br C_6H_4	4-Br C_6H_4	4	76
16	4-Br C_6H_4	C_6H_5	3.5	78
17	C_5H_3S	$C_6H_5CH_2$	3	71

Reaction condition: Mole ratio. Amine: Benzaldehyde: Benzil: Ammonium acetate is 1:1:1:1
Catalyst: 250mg (K10Ti)

[a] Yields refer to isolated pure products.

2.2.5.2.4 *Recycling Studies*

After the reaction the catalyst was filtered, washed with acetone and dried in air oven for 2h at 200°C and reused. The catalyst was found to be active for three cycles. No appreciable loss in yield was observed. The results are summarized in table 2. 7

Table 2.7 Recylcing studies of the catalyst

No.of recycling	Yield %[a]
1	78
2	76
3	73
4	70
5	62

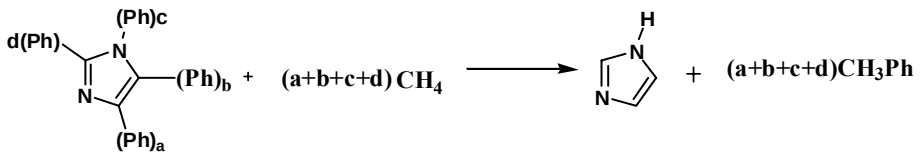
Reaction condition: Benzaldehyde (2 mmol), Benzil (2 mmol), Ammonium acetate (2 mmol)
Catalyst: 250 mg (K10Ti)
[a] Yield refers to isolated pure product

2.2.5.3 Theoretical studies

Density functional theory (DFT) has emerged as a reliable theoretical method to calculate geometries of molecules. Hence, it has been used to evaluate the heats of formation of interested molecules and the results indicate that DFT is a reliable method [48–50]. Nowadays, the DFT methods, especially the B3LYP hybrid DFT method that not only produces reliable geometries and energies but also requires less time and computer resources, have been widely employed and have become an important and economical tool to deal with complex electron correlation problems [51–54]. The geometries of pyrazole and imidazole as well as those of their *N*-methyl, *N*-ethyl, *N*-phenyl, and *N*-benzyl derivatives were optimized at the B3LYP/6-31G (d) level, which was shown to yield quite reliable geometries for these kinds of systems [55]. The B3LYP approach is a density functional hybrid

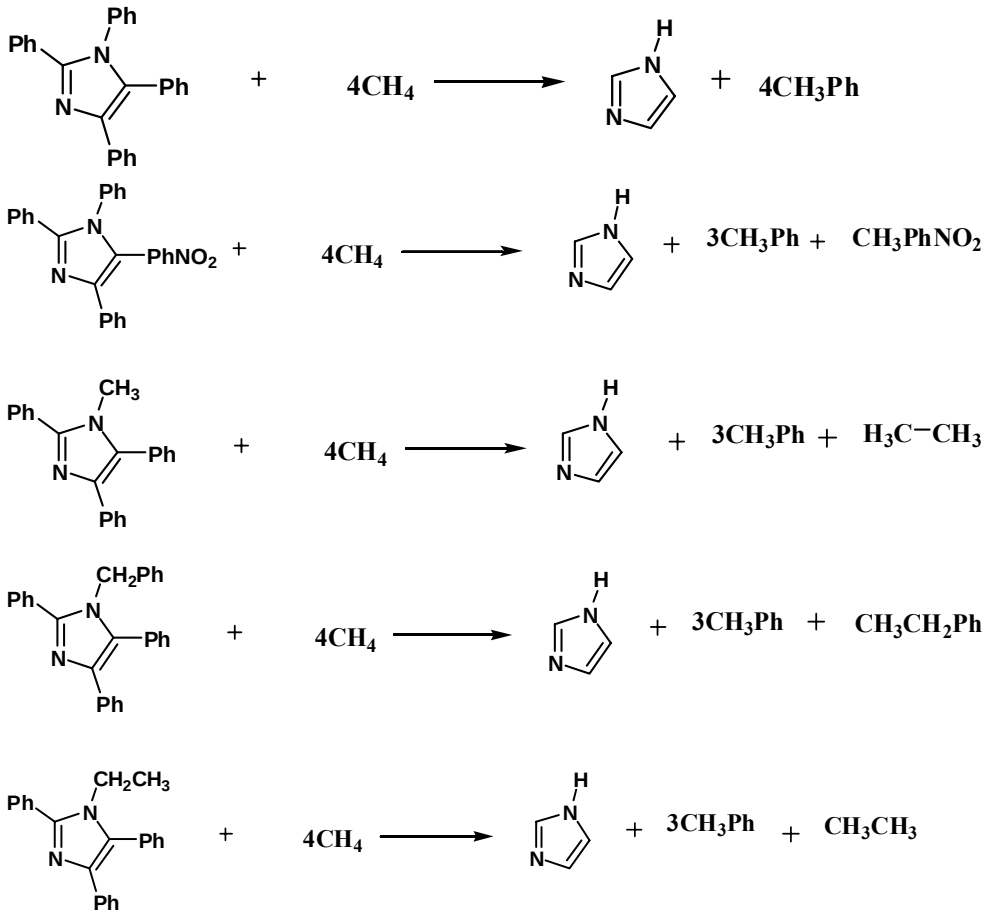
method which combines the Becke's three parameter nonlocal hybrid exchange potential [56, 57] with the nonlocal correlation functional of Lee, Yang, and Parr [58].

Here heat of formation of few tetrasubstituted imidazoles were calculated using density functional theory B3LYP method with 6-31G (d,p) basis set via designed isodesmic reactions. The relationship between structure and heat of formation and yield was studied. The isodesmic reactions were adopted for the prediction of HOFs [59-63]. To compensate for some of the systematic errors, isodesmic reactions are used. The so-called isodesmic reaction processes, in which the number of each kind of formal bond is conserved, are used with application of the bond separation reaction (BSR) rules. The molecule is broken down into a set of two heavy-atom molecules containing the same component bonds. The method of isodesmic reactions has been employed very successfully to calculate HOF from total energies obtained from ab initio calculations. However, usual bond separation reaction rules cannot be applied to the molecules with delocalized bonds and cyclic skeletons because of large calculation errors of HOFs. To be specific, we reserved the conjugated ring and took imidazole as a reference compound (the experimental heat of formation of imidazole is 31.8 k cal/mol in the gas phase). This approach has been proved reliable [64, 59]. The HOFs of the tetra substituted imidazoles at 298 K were calculated from the following isodesmic reactions:



..(1)

Isodesmic reactions studied for some selected compounds



For the isodesmic reaction (1), we have calculated the heat of reaction ΔH_{298} at 298 K from the following equation:

$$\Delta H_{298} = \Sigma \Delta H_{f,p} - \Sigma \Delta H_{f,r} \quad \text{.....(2)}$$

Where $\Delta H_{f,r}$ and $\Delta H_{f,p}$ are the HOFs of reactants and products at 298 K, respectively. The experimental heat of formation of reference compounds CH_4, $C_3H_4N_2$ (imidazole) and side products are available in the literature. The HOFs of imidazole derivatives can be figured out when the heat of reaction ΔH_{298} is

known. Therefore, the most important thing is to calculate ΔH_{298}. It can be calculated using the following expression

$$\Delta H_{298}=\Delta E_{298} +\Delta (PV) = \Delta E_0+\Delta ZPE+\Delta H_T +\Delta nRT \quad \text{.....(3)}$$

Where ΔE_0 is the change in total energy between the products and reactants at 0K; ΔZPE is the difference between the zero-point energies (ZPE) of the products and the reactants; ΔH_T is thermal correction from 0 to 298 K. The Δ (PV) value in Eq. (3) is the PV work term. It equals ΔnRT for the reaction of ideal gases. For the isodesmic reactions (1), Δn = 0, so ΔnRT = 0.

The optimized structure of one of the product was shown in Fig 2.8

Table 2.8 Zero point energy (ZPE), values of thermal correction (H_T) and heat of formation of the title compounds

	ZPE	E	H	H_f(kcal/mol)
TSI 1(Entry 1)	-1150.04	-1150.02	-1150.22	151.36
TSI 2 (Entry 7)	-1354.55	-1354.52	-1354.52	155.78
TSI 3 (Entry 5)	-958.36	-958.34	-958.34	119.4
TSI 4 (Entry 4)	-1189.33	-1189.30	-1189.3	146.53
TSI 5(Entry 10)	-997.65	-997.63	-997.63	114.38

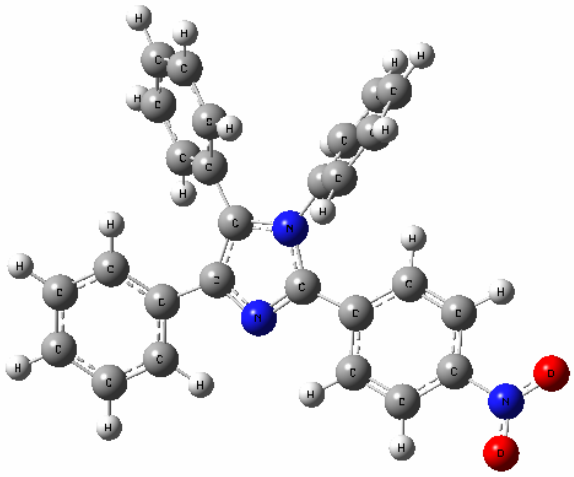


Fig.2.8 Optimized structure of TSI 2 using B3LYP/6-31G (d, p)

2.2.5.3.1 *Correlation between structure and yield of tetrasubstituted imidazoles*

An attempt was made to correlate between structures; HOF and reactivity of the selected imidazoles. The heat of formation for TSI 3 and TSI 5 are comparable. Maximum heat of formation was observed for TSI 2 which was highly substituted with an aromatic ring with electron withdrawing group, which was comparable with TSI 1 and TSI 4. Experimental yield of the TSI 1, TSI 2 and TSI 4 are 78%, 81% and 84 % and those of TSI 3 and TSI 5 with one aliphatic substitution are 68 % and 72 % are comparable.

2.2.5.4 Conclusion

A series of catalysts were prepared, characterized by various physical and chemical techniques. The prepared catalysts were screened for the solvent free synthesis of tetrasubstituted imidazoles. K10 supported Ti catalyst was found to be more active than the other catalysts. The method studied was found to be effective in terms of green chemistry i.e solvent free synthesis. Recycling studies showed that the catalyst was found to be active over three cycles. Theoretical studies of some selected tetrasubstituted imidazoles using designed isodesmic reactions revealed that there was correlation between the structure, heat of formation and yield of substituted imidazoles.

2.2.6 Mannich Reaction

Mannich reactions are among the most important carbon-carbon bond forming reactions in organic synthesis [65-67]. They provide β-amino carbonyl compounds, which are important synthetic intermediates for various pharmaceuticals and natural products [68, 69]. The increasing popularity of the mannich reaction has been fueled by the ubiquitous nature of nitrogen containing compounds in drugs and natural products [70, 71]. However, the classical mannich reaction is plagued by a number of serious disadvantages and has limited applications. Therefore, numerous modern versions of the

mannich reaction have been developed to overcome the drawbacks of the classical method. In general, the improved methodology relies on the two-component system using preformed electrophiles, such as imines, and stable nucleophiles, such as enolates, enol ethers, and enamines [72-76]. But the preferable route is the use of a one-pot three-component strategy that allows for a wide range of structural variations. Ollevier et al. reported that bismuth triflate catalyzed the mannich-type reaction of a variety of in situ generated aldimines using aldehydes, anilines, and silyl enol ethers in a three component reaction [77]. There are only very few reports on clay catalysed mannich reaction [78]. Various catalysts were screened, among them best result was obtained for K10Ti. Synthesis and factors affecting the formation of mannich base are discussed in the forthcoming sections.

2.2.6.1 Mannich Reaction Catalysed by K10Ti

The mannich reaction was carried out reacting cyclohexanone, aldehye and aniline and the catalyst K10Ti (500 mg), the reaction was carried out at room temperature using ethanol as the solvent. After completion of the reaction the mixture was filtered and extracted with ethyl acetate. Pure product was obtained from column chromatography using hexane: ethyl acetate as eluent (8:2 v/v).

2.2.6.2 Effect of catalyst loading

Influence of the amount of catalyst on three component Mannich reaction is studied by taking benzaldehyde, aniline and cyclohexanone in ethanol and the amount of catalyst was varied. The yield was found to increase up to 300mg of the catalyst. Further increase in the amount of the catalyst did not affect the yield of the reaction. Optimum catalyst concentration (300mg) was selected for further studies. The results are summarized in Table 2.9.

Table 2.9 Effect of catalyst loading on Mannich reaction

Sl.No	Amount of catalyst	Time(h)	% Yield[a,b]
1	100	24	48
2	150	24	56
3	200	24	68
4	250	24	70
5	300	24	72
6	350	24	72

[a]Reaction condition: benzaldehyde (3 mmol), aniline (3.1 mmol) and cyclohexanone (5 mmol) Solvent: ethanol, Room temperature
[b]Isolated yield of pure product

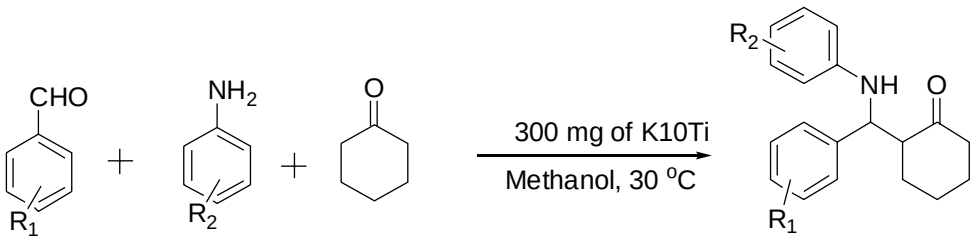
2.2.6.3 Effect of solvent on Mannich reaction

Second factor studied was role of solvents; polar solvents gave good yield, while non polar solvents gave poor yield. The reaction proceeded well in water but a number of products were formed and the products were difficult to be separated, reason may be that water might have been absorbed by the clay which was swollen and side reactions might have taken place. The results are presented in table 2.10. High yield was obtained in methanol. So methanol was selected as solvent for further studies.

Table 2.10 Effect of solvent on Mannich reaction

Entry	Solvent	Time (h)	% Yield [a, b]
1	Ethanol	24	70
2	Methanol	24	72
3	Water	24	65
4	$CHCl_3$	24	68
5	Toluene	24	62

[a]Reaction condition: benzaldehyde (3mmol), aniline (3.1mmol) and cyclohexanone (5mmol) Catalyst: 300 mg K10Ti, room temperature
[b] Isolated yield of pure product



Scheme 3 Three component Mannich reaction catalyzed by Montmorillonite K10 clay supported Ti Catalysts

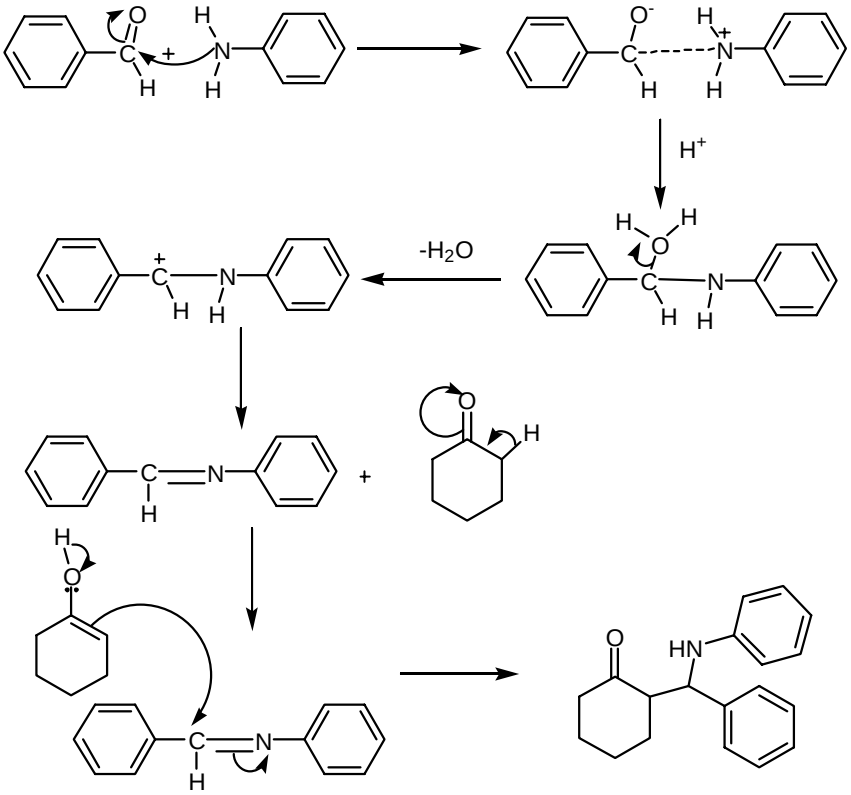
The reliability the reaction was checked with different aldehydes and amines. With all the substrates studied good yields were obtained. The results are summarized in table 2.11

Table 2.11 Mannich reaction catalysed by K10Ti

Entry	R_1	R_2	Ketone	Time (h)	% Yiled[a]
1	H	H	Cyclohexanone	24	74
2	4-Cl	H	Cyclohexanone	20	69
3	4-OCH_3	H	Cyclohexanone	14	71
4	H	4-Br	Cyclohexanone	18	72
5	4-NO_2	4-OCH_3	Cyclohexanone	16	67
6	4-NO_2	H	Cyclohexanone	20	68
7	4-Br	4-OCH_3	Cyclohexanone	22	70
8	H	4-Cl	Cyclohexanone	18	72
9	4-NO_2	H	Cyclohexanone	24	73
10	H	4-OCH_3	Cyclohexanone	18	76
11	Furfural	H	Cyclohexanone	20	73

[a]Reaction condition: aldehyde (3 mmol), amine (3.1 mmol) and cyclohexanone (5 mmol)
Solvent: methanol
Catalyst: 300 mg K10Ti, room temperature
[b] Isolated yield of pure product

2.2.6.4 Mechanism of Mannich reaction



Scheme 2.4 Mechanism of the Mannich reaction

The mechanism can be explained as a Bronsted acid promoted four step process 1) formation of iminium ion 2) enolization 3) C-C bond formation 4) proton transfer. In the presence of acid catalyst aldehyde reacts with amine to form an iminium ion, which upon proton abstraction from the catalyst results in the formation of an ion which reacts with protonated cyclohexanone to give the final product.

The electron withdrawing substituents present on aniline and the electron donating substituents present on aldehydes retard the speed of the reaction and low yield was obtained compared to the other cases. Good yields were obtained for all the substrates studied.

After each set of reaction the catalyst was filtered, washed with ethyl acetate and dried at 150°C for 2h and reused, selecting benzaldehyde, aniline and clyclohexanone as substrates. The activity of the catalyst was decreased gradually (Table 2.12), which may be due to loss of metal ions from the catalyst.

Table 2.12 Recycling studies

Entry	No of cycles	Yield %
1	1	74
2	2	71
3	3	65
4	4	61

Yield refers to isolated pure product
Reaction condition: benzaldehyde (3 mmol), aniline (3.1 mmol), cyclohexanone (5 mmol)
Solvent: Methanol, Catalyst: K10Ti 300 mg
Recation time: 24 h

2.3 Experimental

2.3.1 Preparation of titanium containing catalysts

The Montmorillonite K10 and Montmorillonite KSF clay samples were activated overnight at 100^0C. 3 g of activated clay suspended in 50 ml chloroform was stirred at room temperature in N_2 atm for about 30 min. 2 ml of triethyl amine was added to activate the surface silanol groups and the slurry was stirred for 30 minutes. Titanocene dichloride (0.6g) dissolved in $CHCl_3$ was added under stirring under N_2 atmosphere. The slurry was stirred until the color of the suspension was changed from red to yellow over a period of 3 h. This was washed with $CHCl_3$ (30mlx 5 times). After washing, the solids recovered were calcined and dried at 500^0C for 8h.

2.3.2 Preparation of Na^+, Co^{3+}, Cu^{2+} exchanged Montmorillonite K10 and Montmorillonite KSF Catalysts

Sodium exchanged clay was prepared by weighing 1.5 g activated clay which was stirred with 0.5 M $NaNO_3$ solution(20ml) overnight and washed

with water until the filtrate was free from chloride ions and dried in an air oven at 200^0C. The Co and Cu exchanged clays were prepared by stirring 3g each of sodium exchanged clay with 25ml of 1M solution of Cobalt(II)Chloride and Cu (II)Chloride for 24h. The solution was filtered and washed with (50ml x 5 times) water until the filtrate was free from chloride ions. The catalyst was dried at 200°C for 2h.

2.3.3 Synthesis of tetrasubstituted imidazoles

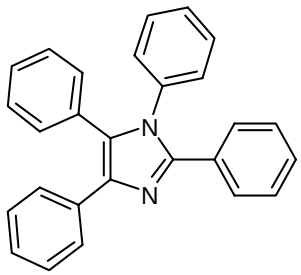
Synthesis was carried out by reacting, benzil (421 mg, 2 mmol), aldehyde (2 mmol), amine (2 mmol), ammonium acetate (309 mg, 2 mmol) and 250 mg of the catalyst. The reaction mixture was stirred at 120°C. The reaction was monitored by TLC on silica gel coated plate, with 9:1 mixture of hexane and ethyl acetate. After completion of the reaction, the crude product was separated by extraction using ethyl acetate followed by filtration. Finally the pure product was isolated by column chromatography on small silica column using hexane and ethyl acetae (9:1 v/v) as eluent. All the products were known compounds and were characterized by FT-IR, ^{1}H NMR spectral analysis.

2.3.4 Three component mannich reaction

A 10 mL round bottom flask was charged with aldehyde (3 mmol), aniline (3.1 mmol) ketone (5 mmol), ethanol (5 mL) and 300 mg K10Ti catalyst. The reaction mixture was stirred at room temperature. The progress of the reaction was followed using thin layer chromatography on silica gel plate using hexane: ethyl acetate mixture (20:1 v/v) as eluent. After the completion of the reaction, the catalyst was filtered and washed with ethyl acetate. The filtrate and washings were combined and evaporated to remove the solvent. The final product was isolated by column chromatography on silica gel using hexane-ethyl acetate mixture (20:1 v/v) as the eluent. The yield of the product was noted. The β-amino ketones were characterized by FTIR and ^{1}HNMR spectroscopy

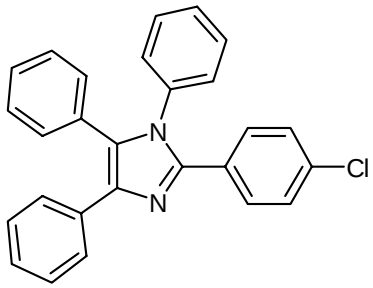
2.3.5 Characterization of the products

2.3.5.1 Tetrasubstituted imidazoles



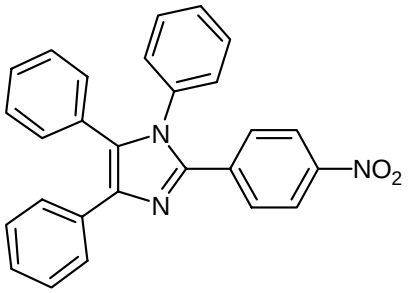
1,2,4,5-tetraphenyl-1*H*-imidazole

(Entry 1 Table 2.6), (lit.,[79] Mp: 220°C); IR υ_{max}(cm^{-1}):2986(C-H), 1600(C=C), 1580(C=N), ^{1}H NMR,(300 MHz, $CDCl_3$);δ(ppm); δ 6.80-7.60(m, ArH)



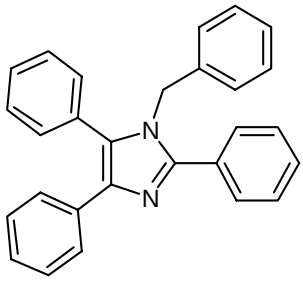
2-(4-chlorophenyl)-1,4,5-triphenyl-1*H*-imidazole

(Entry 2 Table 2.6), (lit.,[79] Mp: 105°C); IR υ_{max} (cm^{-1}): 2982(C-H), 1589(C=C), 1574(C=N), ^{1}H NMR, (300 MHz, $CDCl_3$); δ (ppm); δ 7.01-7.28(m, 15H) 7.34-7.59 (dd, 4H J= 7.8Hz)



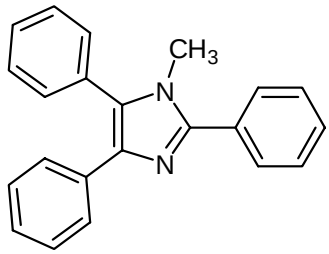
2-(4-nitrophenyl)-1,4,5-triphenyl-1*H*-imidazole

(Entry 3 Table 2.6), (lit.,[32] Mp: 255°C); IR υ_{max} (cm^{-1}): 2987(C-H), 1604(C=C), 1510(C=N), ^{1}H NMR,(400 MHz, $CDCl_3$);δ(ppm); δ7.01-7.45 (m,15H, Ph) 7.58(d,1H, J=8.3 H_Z) 7.81(d, 1H, J=7.8Hz), 8.0-8.2 (d, 1H, J=8.1 Hz) 8.24 (d, 1H J=8.6Hz).



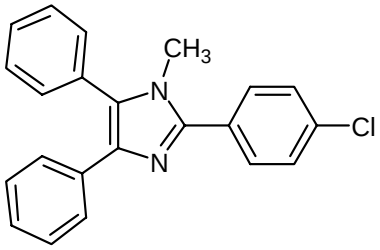
1-benzyl-2, 4, 5-triphenyl-1H-imidazole

(Entry 4 Table 2.6), (lit.,[80] Mp: 168°C; IR υ_{max} (cm^{-1}): 2982(C-H), 1600(C=C), 1574(C=N), ^{1}H NMR, (400 MHz, $CDCl_3$); δ (ppm); 6.79-7.66(20H, m, Ar-H), 5.10(2H, s, CH_2).



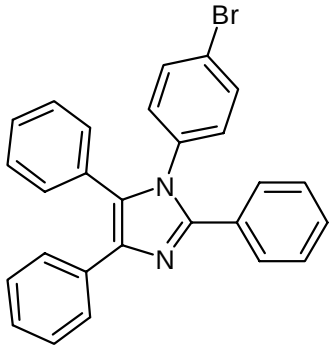
1-methyl-2,4,5-triphenyl-1H-imidazole

(Entry 5 Table 2.6), (lit.,[80] Mp): 142°C; IR υ_{max} (cm^{-1}): 2889(C-H), 1602(C=C), 1531(C=N), ^{1}H NMR, (300 MHz, $CDCl_3$); δ (ppm); δ7.12-7.76(m, 15H), 3.51(s, 3H)



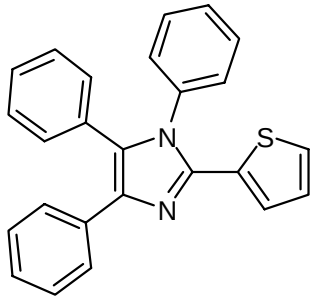
2-(4-chlorophenyl)-1-methyl-4, 5-diphenyl-1H-imidazole

(Entry 6 Table 2.6), Mp: 172°C; IR υ_{max} (cm^{-1}):2982(C-H), 1592(C=C), 1530(C=N), ^{1}H NMR, (400 MHz, $CDCl_3$);δ(ppm); 7.12-8.50(14H,m Ar-H), 3.35(3H,s)



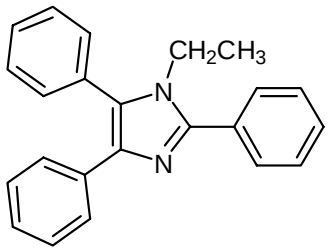
1-(4-bromophenyl)-2,4,5-triphenyl-1*H*-imidazole

(Entry 8 Table 2.6), Mp: 168°C; IR υ_{max} (cm^{-1}):2986(C-H), 1592(C=C), 1477(C=N), ^{1}H NMR, (400 MHz, $CDCl_3$); δ (ppm); 7.20-7.60 (15H, m, Ar-H) 7.10-7.15(dd, 2H), 6.87-6.92(d, 2H, J=8.6Hz)



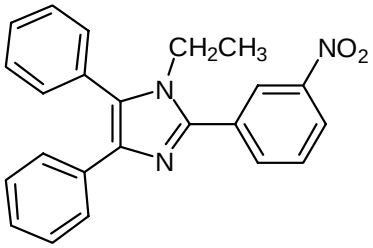
1,4,5-triphenyl-2-(thiophen-2-yl)-1*H*-imidazole

(Entry 9 Table 2.6), (lit.,[79] Mp: 162°C); IR υ_{max} (cm^{-1}):2986(C-H), 1600(C=C), 1574(C=N), ^{1}H NMR, (400 MHz, $CDCl_3$); δ (ppm); 7.06-7.89(16H, m, Ar-H), 6.70(b, 1H) 6.83(t, 1H).



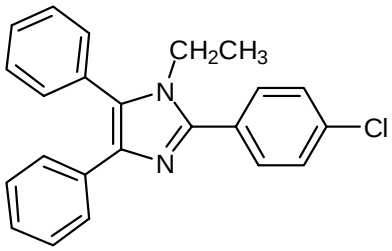
1-ethyl-2,4,5-triphenyl-1*H*-imidazole

(Entry 10 Table 2.6), (lit.,[80] Mp): 168°C; IR υ_{max} (cm^{-1}):2985(C-H), 1600(C=C), 1574(C=N), ^{1}H NMR, (300 MHz, $CDCl_3$); δ (ppm); 7.10-8.09 (15H, m, Ar-H), 3.91(2H, q, J=6.9Hz) 1.01(3H, t, J=7.18Hz)



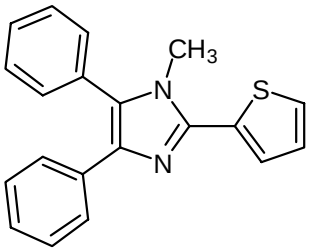
1-ethyl-2-(3-nitrophenyl)-4,5-diphenyl-1*H*-imidazole

(Entry 11 Table 2.6), Mp: 166°C; IR υ_{max} (cm^{-1}):2982(C-H), 1605(C=C), 1510(C=N), ^{1}H NMR, (400 MHz, $CDCl_3$); δ (ppm); 7.14-8.60(19H, m, Ar-H), 3.96 (2H, q, J=7.14) 0.95 (3H, t, J=7.02Hz)



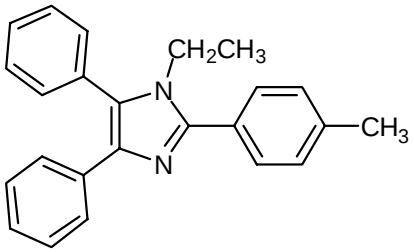
2-(4-chlorophenyl)-1-ethyl-4,5-diphenyl-1*H*-imidazole

(Entry 12 Table 2.6), Mp: 126°C; IR υ_{max} (cm^{-1}):2990(C-H), 1604(C=C), 1572(C=N), ^{1}H NMR, (400 MHz, $CDCl_3$); δ (ppm); 7.0-7.8(14H, m, Ar-H), 4.2(2H, q, J=7.13Hz) 1.10 (3H, t, J=7.32Hz)



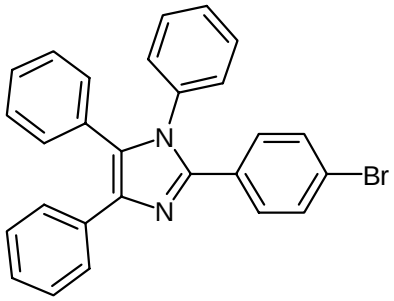
1-methyl-4,5-diphenyl-2-(thiophen-2-yl)-1*H*-imidazole

(Entry 13 Table 2.6), Mp: 247°C; IR υ_{max} (cm^{-1}):2990(C-H), 1604(C=C), 1479(C=N), ^{1}H NMR, (400 MHz, $CDCl_3$); δ (ppm); 7.15-7.97(13H, m, Ar-H), 3.62(3H, s)



1-ethyl-4,5-diphenyl-2-p-tolyl-1H-imidazole

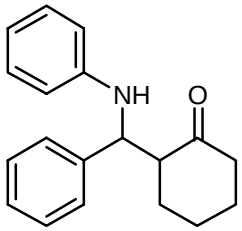
(Entry 14 Table 2.6), Mp: 188°C; IR υ_{max} (cm^{-1}): 2982(C-H), 1600(C=C), 1574(C=N), ^{1}H NMR, (400 MHz, $CDCl_3$); δ(ppm);1.62(t, 3H), 3.73(q, 2H), 2.15(3H, s, CH_3), 6.92-7.73(14H, m, Ar-H)



2-(4-bromophenyl)-1,4,5-triphenyl-1*H*-imidazole

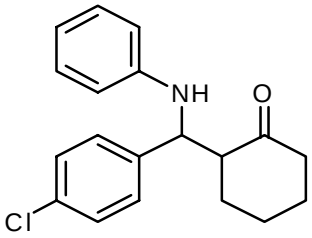
(Entry 16 Table 2.6), Mp: 168°C; IR υ_{max} (cm^{-1}):2975(C-H), 1600(C=C), 1574(C=N), ^{1}H NMR, (400 MHz, $CDCl_3$); δ (ppm); 7.94(d, 2H), 7.12-7.40(m, 17H)

2.3.5.2 Mannich bases



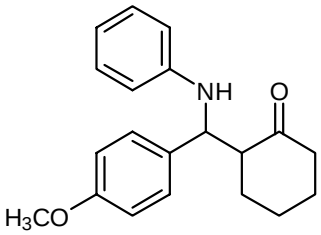
2-[1'-(N-phenylamino)-1'-(4-phenyl)]methylcyclohexanone

(Entry 1 table 2.11) FTIR (KBr, ν_{max} (cm^{-1})): 3383, 1696;
^{1}HNMR ($CDCl_3$ 400MHz): δ 7.43 (d, J = 7.9 Hz, 2H, Ar-H), 7.33-7.37 (m, 2H, Ar-H), 7.18-7.23 (m, 1H, Ar-H), 7.05-7.09 (m, 2H, Ar-H), 6.65-6.61 (m, 1H, Ar-H), 6.56 (d, J = 7.2 Hz, 2H, Ar-H), 4.62 (brs, 1H), 2.83,(q,1H), 2.71-2.76 (m, 1H), 2.32-2.45 (m, 2H), 1.59-1.86 (m, 6H).



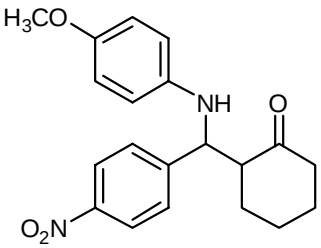
2-[1'-(N-phenylamino)-1'-(4-chlorophenyl)]methylcyclohexanone

(Entry 2 table 2. 11) FTIR (KBr, ν_{max} (cm^{-1})) 3390, 3119, 1712, 1142, 1090; ^{1}HNMR ($CDCl_3$, 400 MHz): δ 7.31-7.26 (m, 2H), 7.25-7.23 (m, 2H), 7.07-7.03 (m, 2H), 6.63 (m, 1H), 6.53-6.46 (m, 2H), 4.68 (br, 1H), 4.59 (d, *J* =6.6 Hz, 1H), 2.73-2.71 (m, 1H), 2.43-2.38 (m, 1H), 2.32-2.31 (m, 1H), 1.91-1.84 (m, 3H), 1.70-1.57 (m, 3H).



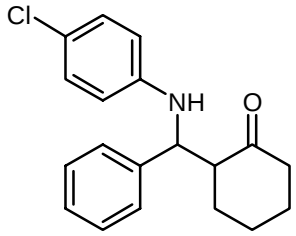
2-[1'-(N-phenylamino)-1'-(4-methoxyphenyl)]methylcyclohexanone

(Entry 3 table 2. 11) FTIR (KBr, ν_{max} (cm^{-1})): 3364, 2935, 1706, 1604, 1512; ^{1}H NMR (400MHz, $CDCl_3$): δ7.19-7.36 (5H, m), 6.62-6.67 (2H, m), 6.47-6.52 (2H, m), 4.73 (br, s, 1H), 4.63 (d, 1H, J = 7.2 Hz), 4.5 (br, 1H), 3.65 (s, 3H), 2.71-2.72 (1H, m), 2.31-2.43 (2H, m), 1.61-1.88 (6H, m).



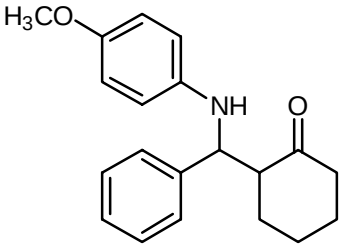
2-[1'-(N-methoxy phenylamino)-1'-(4-nitrophenyl)]methylcyclohexanone

(Entry 4 table 2. 11) FTIR (KBr, ν_{max} (cm^{-1})) 3402, 2956, 1702, 1608, ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.2 (d,2H, *J* =8.6 Hz), 7.55 (d, 2H, *J* =8.6 Hz), 6.66 (d, 2 H, *J* =8.8 Hz), 6.43 (d, 2 H, *J* =8.8 Hz), 4.79 (d, 1 H, *J* =4.4 Hz), 4.38 (br s,1H), 3.66 (s, 3H), 2.81 (m, 1H), 2.38 (m, 2 H), 2.23 (m, 2H), 1.59–2.21 (m, 4H).



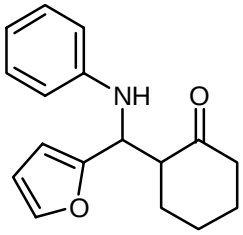
2-[1'-(N-p-chlorophenylamino)-1'-(4-phenyl)]methylcyclohexanone

(Entry 8 table 2. 11) FTIR (KBr, ν_{max} (cm^{-1})): 3378, 1674. ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ7.56 (d, J = 8.9 Hz, 2H, Ar-H), 7.41-7.48 (m, 2H, Ar-H), 7.22-7.17 (m, 1H, Ar-H), 6.98 (d, J = 8.7 Hz, 2H, Ar-H), 6.58 (d, J = 7.3 Hz, 2H, Ar-H), 4.56 (brs, 1H), 2.65-2.61 (m, 1H), 2.28-2.31 (m, 2H), 1.60-1.92 (m, 6H).



2-[1'-(N-p-methoxyphenylamino)-1'-(4-phenyl)]methylcyclohexanone

(Entry 10 table 2. 11) FTIR (KBr, ν_{max} (cm^{-1})): 3332, 1690. ^{1}H NMR (400 MHz, TMS, $CDCl_3$): δ7.27 (d, J = 8.4 Hz, 2H, Ar-H), 7.16 (d, J = 7.6 Hz, 2H, Ar-H), 7.10-7.03 (m, 2H, Ar-H), 6.68 (d, J = 8.3 Hz, 2H, Ar-H), 6.64-6.61 (m, 1H, Ar-H), 4.73 (br, s, 1H), 4.63 (d, J = 7.2 Hz, 1H), 3.89 (s, 3H, OCH_3), 2.72-2.76 (m, 1H), 2.42-2.47 (m, 2H), 1.68-1.93 (m, 6H).



2-[1'-(N-p-methoxyphenylamino)-1'-(2-furyl)]methylcyclohexanone

(Entry 11 table 2. 11) FTIR (KBr, ν_{max} (cm^{-1})): 3362, 2938, 1673, 1597, 1500; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10-7.29 (3H, m), 6.61-6.71 (3H, m), 6.17-6.26 (2H, m), 4.87 (0.33H, d, *J* = 4.7 Hz), 4.81 (0.67H, d, *J* = 5.3 Hz), 4.5 (1H, br), 2.89-2.99 (1H, m), 1.60-2.40 (8H, m).

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Chapter 3

ALUMINIUM PILLARED SAPNONITE: PREPARATION, CHARACTERIZATION AND CATALYTIC APPLICATION

Contents

Pillaring is the process of insertion of metals or metal oxides between the clay layers so as to increase the interlayer spacing of the catalyst to effect the reactant to diffuse in to the channels more efficiently and to give better results in pillared catalyst assisted organic synthesis. Preparation of pillared saponite, its characterization and use in acetal formation of pentaerithritol is discussed in this chapter.

3.1 Introduction

Naturally occurring and synthetic clays, which are usually rich in exchangeable Na^+, K^+, or Ca^{2+} cations can be converted into viable catalysts by directly or indirectly inserting protons in the interlamellar region. Such catalysts still suffer from the disadvantage of physical collapse at high temperature. At 470K, the interlamellar solvent species (water or reacting

organic layer) tend to be expelled, and therefore, sustaining catalytic activity of the clay at higher temperatures is by inserting pillars, preferably of inorganic character, which serve to keep the individual layers apart. There is usually a chemical bond between aluminosilicate layer and the pillar, making this step more or less irreversible. The generation of pillared clays has other advantages, not the least among them being the merit of incorporating extra 'pores' into the catalyst. Where it is possible to space the pillars evenly, and in a controllable fashion, a new type of shape selective catalyst would be produced.

The synthesis of metal oxide pillared interlayer clays (PILCs) was first reported in the late seventies as a new group of microporous materials with larger pore size, but lower (hydro)thermal stability than zeolites [1–3]. Pillared clays (PILCs) are two-dimensional zeolite-like materials prepared by exchanging charge compensating cations between the clay layers with large inorganic metal hydroxycations, which are oligomeric and are formed by hydrolysis of metal oxides or salts [4]. After calcination, the metal hydroxy cations are decomposed into oxide pillars that keep the clay layers apart and create interlayer and inter pillar spaces, thereby exposing the internal surfaces of the clay layers. Baes and Meisner, Burch, etc. had reported that, in principle, any metal oxide or salt that forms polynuclear species upon hydrolysis can be inserted as a pillar [5–7]. Sychev et al. has studied the micropore structure of Cr and Ti-pillared clays with different pillar density by N_2, water and benzene adsorption [8, 9]. Change in pillar density results in a change in all the physical characteristics such as surface area, pore volume and the pore size distribution of the pillared clays. This fact has been established by applying several theoretical approaches to the adsorption data of N_2, water and benzene adsorption on these pillared clays [8, 9].

A great number of works deal with characterization of acidic properties of clays, although increasingly criticized [10]. PILCs possess both Brønsted acid

(proton donor) sites and Lewis acid (electron pair acceptor) sites [11, 12]. Generally, it is believed that Brønsted acidity is mainly coming from the clay layer structural hydroxyl groups, while Lewis acidity is attributed to the metal oxide pillars. In addition, the amount and strength of Brønsted and Lewis acid sites are closely related to the types of clays and metal oxide pillars. For example, when montmorillonite is compared to beidellite and saponite, both Al- and Ti-pillared beidellite [13] and Al-pillared saponite [14] show higher Brønsted acidity than Al- or Ti-pillared Montmorillonite. The reason for this higher Brønsted acidity is the high extent of replacement of Si^{4+} by Al^{3+} in the tetrahedral silicate sheets in beidellite and saponite, and the proton attack of these substituted sites results in the generation of Si-OH · · · Al substrates, which are present as Brønsted acid sites [13–14]. Ming–Yuan showed that the same montmorillonite pillared by different metal oxides exhibit differences in acidity, with the highest acidity for Ti-PILC and the lowest for Ni-PILC [15]. The acidity shown in this study is mainly attributed to Lewis acidity. It should be noted that heating process also has strong influence on the acidity of PILC. Normally, Lewis acidity is more thermally stable than Brønsted acidity. However, upon increasing the calcination temperature, both Lewis and Brønsted acidities will decrease.

PILCs are microporous materials. For an ideal PILC, such as Al-PILC, the micropore is defined by the interlayer distance, which is the space between the clay layers, and lateral distance, which is the space between the metal oxide pillars, as illustrated in Fig. 3.1 (a). Generally PILCs exhibit bimodal pore size distribution with pore size bigger than zeolites, which show advantages in reactions with larger molecules. In the acid catalytic applications, the porous structure of PILCs, always associated with the surface acidity, will determine the type of reactions and also the total conversion and product selectivity.

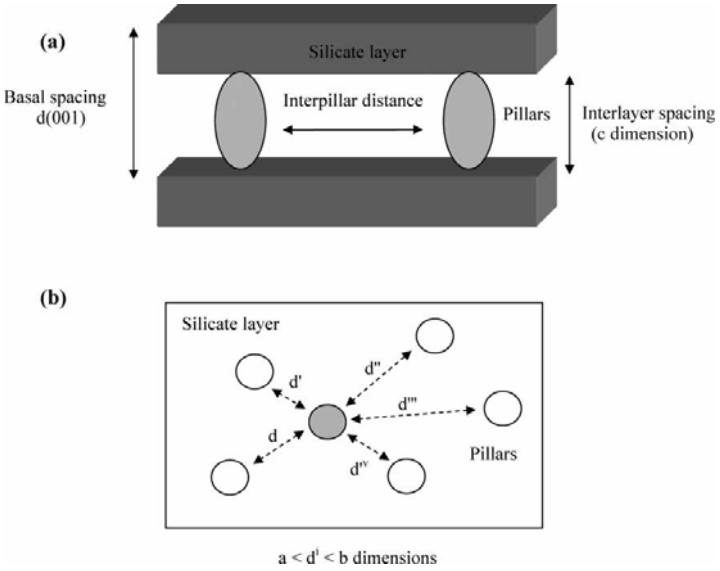


Fig. 3.1 Schematic representation of the microstructure of pillared inter layered clays (PILCs), with indication of some characteristic parameters: (a) side view; (b) basal view

In the mid 1930's, acid modified smectite-type of clays were widely used as commercial catalysts in petroleum-cracking reaction. Around the mid 1960's, the role of acidic clays in cracking process was taken over by Y zeolites and aluminosilicates with better thermal stability and shape selectivity. However, new reports on the successful synthesis of PILCs using inorganic complexes have renewed the interests in applying them as catalysts in various reactions [16-18]. In addition to the use of PILCs in catalytic cracking processes, the application of PILCs as acid catalysts in the synthesis of fine chemicals forms another interesting area. Different types of reactions have been studied, such as hydroisomerisation [19–22], dehydration [23–25], dehydrogenation [26, 27], hydrogenation [28, 29], aromatization [30], disproportionation [31, 32], esterification [33], alkylation [34, 35], etc. The reaction conditions are milder than that in cracking processes and the product selectivity is dependent on the type and strength of the acidity and the pore geometry of PILCs. Some examples are given in Table 3.1

Table 3.1 Various Organic reactions on pillared clays

Reaction	Substrate → Product	PILC Catalyst	Important parameter	Ref
Dehydration	2-propanol → propene, methanol → hydrocarbons Pentan-1-ol → pentenes 1-butanol → butene isomers	Cr-PILC Al/ Al-PILC Ti-PILC	Brønsted acidity Proton content Surface acidity	[36] [37] [38]
Disproportionation	Propene → ethene, 2-butene, 1-butene	Mo/Al-PILC	Brønsted acidity, Lewis acidity, Mo active sites	[39, 40]
Aromatic nitration	Chlorobenzene → nitrochlorobenzene	Fe-(or Cr-or Mn-) PILC	Brønsted acidity, transition metal	[41]
Esterification	acetic acid, 2-methoxyethanol → 2-methoxyethanol acetate	Al-PILC	Lewis acidity	[42]
Isomerisation	1-butene → iso-butane, iso-butene	Al-PILC	Brønsted acidity	[43]
Fischer–Tropsch synthesis	CO, H_2 → highly isomerised hydrocarbons (branched alkanes and internal alkenes)	Ru /Al-PILC	Brønsted acidity	[44]
Phase transfer catalysis	α-tosyloxyketone, → NaN_3 α-azidoketone bromide	Tetramethyl ammonium -PILC	Presence of surfactant for easy access by reactants	[45]
Aromatization	C_3 → benzene,C_4 → xylene	Zn/Al-PILC	weak acidity	[46]
Dehydrogenation	Cyclohexane → benzene Cumene → α-methylstyrene	Cr-PILC	Large gallery height Lewis acidity	[47], [48]

3.1.1 Acetalation of pentaerithritol

Acetalation has widely been used to protect the carbonyl group of aldehydes and ketones. Various kinds of acids are well known to catalyze the reaction in homogeneous and heterogeneous phases [49]. Pentaerythritol is an alcohol with formula $C(CH_2OH)_4$ It is a white, crystalline polyol with the neopentane backbone, a versatile building block for the preparation of many polyfunctional compounds such as pentaerythritol tetraacrylate or the explosive PETN (pentaerythritol tetranitrate). Derivatives of pentaerythritol are components of alkyd resins, varnishes, PVC stabilizers, tall oil esters, and olefin antioxidants. Halogen-free pentaerythritol esters are environmentally friendly alternatives to conventional electrical transformer fluids, being both readily biodegradable and non-hazardous in water. They advantageously replace polychlorobiphenyl (PCB), and even silicone-based or fluorinated hydrocarbons, as their low volatility and high flash point give them an excellent resistance to ignition in case of major electrical failure and transformer rupture [50]. Pentaerithritol acetals are applied as plasticizers and vulcanizers, as physiologically active substances and as potential protective groups for aldehydes and ketones [51]. 1, 2-diacetals are efficient protecting groups for vicinal 1, 2-diol units in carbohydrates [52, 53]. Protection of the carbonyl group of aldehydes and ketones can be accomplished by alcohols [54], diols [55] or trioxanes [56]. Acetonide formation is the most commonly used protection for 1, 2 (*cis*) - and 1, 3-diols, which have extensively been used in carbohydrate chemistry to selectively mask the hydroxyls of different sugars. These reactions are generally effected either with a free carbonyl, aldehyde or ketone [57], or with masked carbonyls (e.g., acetals [58], ketals [59], or enolethers [60] in the presence of a variety of catalysts such as mineral acid [61], formic acid [62], $CuSO_4$ [63], $ZnCl_2$ [64], *p*-toluenesulfonic acid [65], camphorsulfonic acid [66], iodine [67], etc. Besides the interest of acetals as protecting groups, many of them have direct application as fragrances [68, 69], in cosmetics and beverage additives [70, 71].

The most general method for the synthesis of acetals is the reaction between carbonyl compounds and an alcohol or an orthoester in the presence of acid catalysts. The commonly used acid catalysts include corrosive protic acids such as HCl, H_2SO_4 and Lewis acids such as $ZnCl_2$ and $FeCl_3$ [72, 73]. A series of diphosphine complexes have also been employed for the synthesis of acetals [74, 75]. However, acetalation by afore mentioned methods require tedious work-up procedure, chemicals required for the synthesis of complexes are expensive. In this context, the use of heterogeneous acid catalysts for the reaction is attractive and it may allow carrying out the reaction without the generation of water waste. Thus, the use of an Al-pillared saponite is explored and its catalytic activity was studied with acetal formation reaction.

3.2 Results and Discussion

3.2.1 Pillaring of saponite

The first step of pillaring involves treatment of the natural saponite with 0.1M polycation solution of aluminium. Polycation solution of aluminium was prepared by treating 0.5 M solution of aluminium chloride ($AlCl_3.6H_2O$), and NaOH solution to give a final concentration of polycation 0.1 M. The polycations enter in to the interlayer space substituting the interlayer cations. The catalyst was filtered, washed and dried; it is called intercalated clay catalyst. This catalyst is said to be in metastable state, the polycations are not bonded to the clay layers, and they are only fixed by cation exchange. The catalyst is calcined at 500^oC to link the polycations to the clay layers to give the pillared aluminium catalyst.

3.2.2 Characterization

Elemental composition of the saponite and pillared saponite are determined using ICP-AES. It is observed that the percentage composition of SiO_2 decreased while that of alumina was found to increase upon pillaring, the

percentage of rest of the elements only showed a proportional decrease due to fixation of aluminium. The results are given in table 3.2. The intercalation of alumina was successful and fixation of 8.8 wt% Al_2O_3 during the pillaring, Al_{13}^{7+} polycations have substituted Ca^{2+}, Na^{+}, and lower extent K^{+}, the exchangeable cations of the original clay. This was in accordance with the results of previous work on alumina pillared clays [76]. The parent solid is a well-ordered saponite, with a basal spacing of 13.8 Å (Figure 3.1). Its structural formula, deduced from the chemical analysis shown in Table 2, is $[Si_{7.348}\ Al_{0.652}][Al_{0.178}\ Mg_{5.369}\ Mn_{0.004}\ Fe_{0.154}\ Ti_{0.022}]\ O_{20}\ (OH)_4\ [Ca_{0.096}\ Na_{0.66}\ Mg_{0.230}\ K_{0.081}]$.

Table 3.2 Chemical composition of natural and pillared saponite. Results are given on dry-basis, that is, the content of the metallic oxides has been normalized to sum 100%.

Sample	SiO_2	Al_2O_3	Fe_2O_3	MnO	MgO	CaO	Na_2O	K_2O	TiO_2
Saponite	60.09	5.77	1.65	0.03	30.70	0.71	0.27	0.52	0.25
Al-PILC	56.46	14.56	1.51	0.03	26.64	0.11	0.04	0.44	0.22

The process of intercalation-pillaring was successful, giving rise to pillared clay with a basal spacing of 18.48A°, as observed in Figure 3.2. This indicates that the catalyst prepared is a well ordered solid, with its interlayer space considerably increased from 13.8A° to 18.48A° by pillaring. The d spacing of the parent and pillared catalysts are shown in table 3.3. The gallery height for the aluminium pillared saponite is 4.2A° which is much higher than those reported for pillared saponite [76]. All the characteristic peaks of the original clay are maintained in the pillared one, showing that the structure of the layers was not altered; simply they were separated on the *c*-direction.

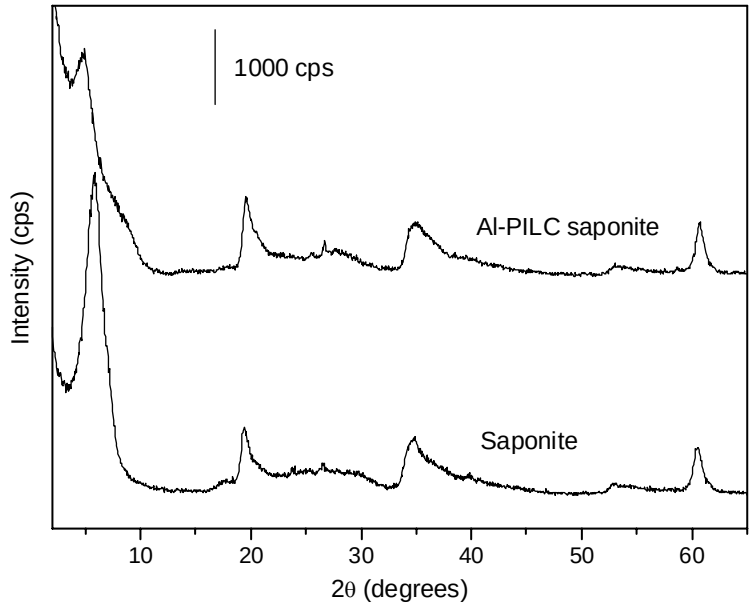


Fig. 3.2 X-ray diffractograms of the parent purified saponite and of the Al-pillared catalyst.

Table 3.3 d spacing of the catalysts

Sample	d_{001} (Å)
Saponite	13.81
Al	18.33
Al-500	18.48

The specific BET surface area of the saponite is 169 m^2/g, which is higher than the values usually reported for natural saponites, but in accordance with those reported for saponites from Madrid Basin. These saponites have a geological sedimentary origin and show small particle size and high surface area values. Upon pillaring, the surface area was increased from 169m^2/g to 274m^2/g from which 218 m^2/g (80%) corresponded to micropore region, showing a correct development of the porous structure of the catalyst during pillaring process. The calcination of the pillared samples was carried out at 200^oC and 500^oC. The results are summarised in Table 3.4.

Table 3.4 Surface area of the catalysts

Sample	Saponite	Al	Al-500
BET surface area (S BET/m^2g^{-1})	169	334	274
L angmuir surface area (S Langmuir/m^2g^{-1})	212	400	358
Surface of micropores (S MP/m^2g^{-1})	111	283	218
External surface area (S EXT/m^2g-1)	57	50	55
Percentage of micropore with respect to Total surface (%SMP)	66	85	80
Pore diameter (Pore diameter/^{0}A)	5.5	6.0	-

The adsorption isotherms of the natural clay is of type II in the Brunauer, Deming, Deming, and Teller (BDDT) classification [37].

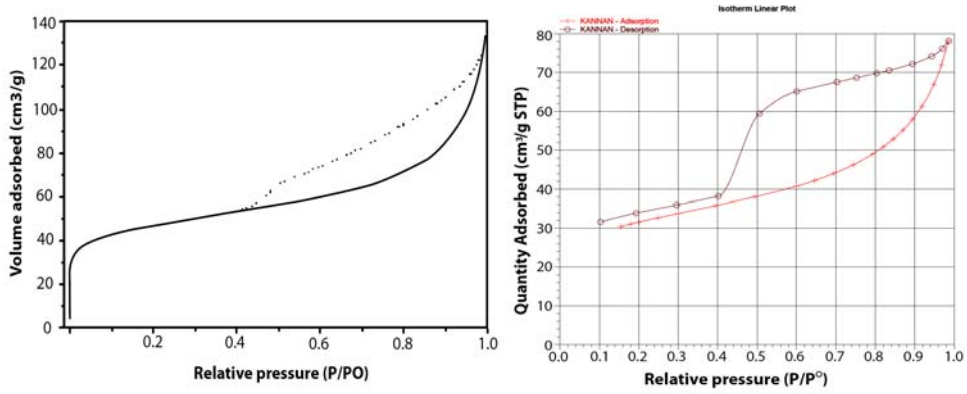


Fig. 3.3 Adsorption isotherm of natural saponite and Al-pillared saponite

FT IR studies of the parent saponite, pillared saponite calcined at 500^{o}C and 200 ^{o}C were performed. The peaks at 1633$cm^{-1}$and 1653cm^{-1} due to the scissoring vibrations of water were decreased in intensity upon increasing the temperature, and it was absent in the sample calcined at 500^{o}C. The peak at 3423cm^{-1} due to bending vibrations of water was decreased in intensity, peak at 3682 cm^{-1} due to Mg-OH str had disappeared upon pillaring and subsequent calcinations.

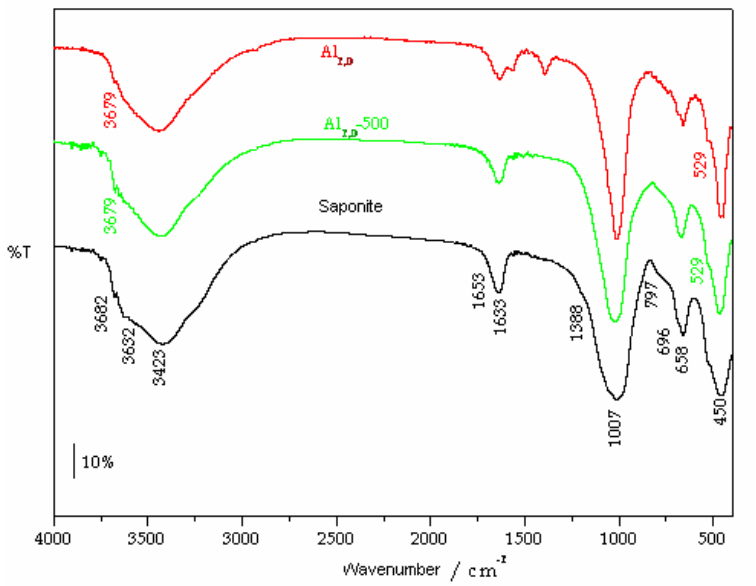


Fig. 3.4 FT IR spectra of the prepared catalyst

The effect of pillaring on the thermal stability was studied by TG-DTA and curves are depicted in Fig 3.5. TG plots of pillared saponite showed a weight loss around 120°C, due to loss of physically adsorbed water. Water loss in this temperature range is an indication for non crystalline hydrated water. Thermogravimetric analysis showed that the catalyst was stable up to 850°C.

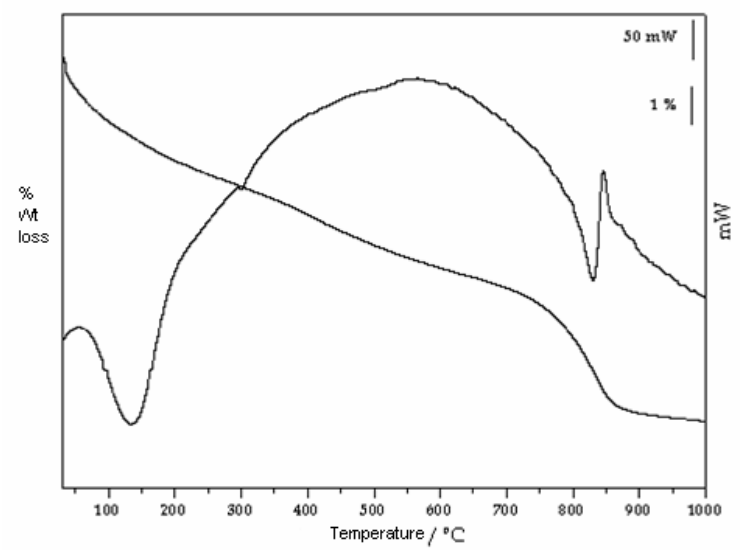


Fig. 3.5 TG/DTA of pillared saponite

Surface morphology of the catalyst was studied by SEM micrograph analysis. It was observed from Fig 3.6 that the surface morphology of the catalyst was maintained upon pillaring.

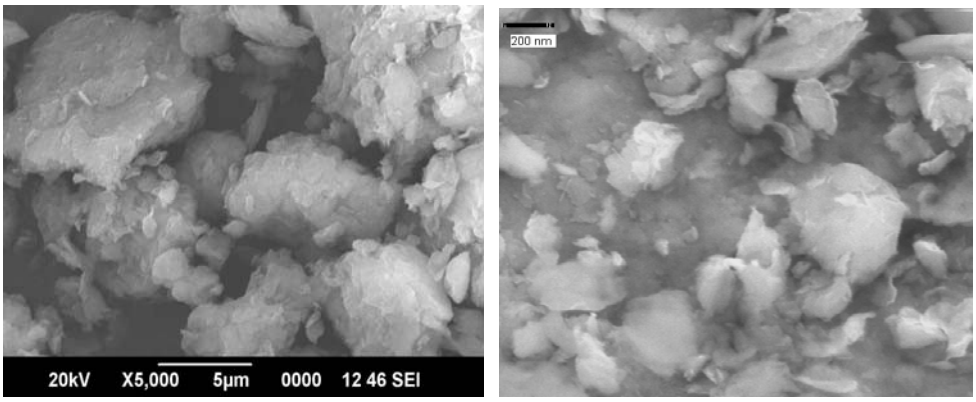


Fig. 3.6 SEM micrograph of natural saponite SEM micrograph of pillared Saponite

The investigation of the surface adidity of Al-PILCs by IR spectroscopy using pyridine as probe molecule has been successfully used in various investigations [77, 78]. The spectra of pillared saponite, before and after pyridine adsorption, are shown in Fig 3.7. The spectra show adsorption bands at 1449, 1492 and 1600cm^{-1}, which are assigned to pyridine molecules interacting with Lewis and Bronsted acid sites of the catalyst. It has been shown in earlier reports that Bronsted acid sites in the vicinity of Lewis acidic metal cente (active sites) act as co-catalyst [79, 80]. The bands at 1449cm^{-1} and 1600cm^{-1} are attributed to pyridine bound to Lewis acid sites (L) [81, 82]. The band at 1492cm^{-1} may be attributed to pyridine associated with both Lewis and Bronsted acid sites (L+B). It is observed that the peak corresponding to Lewis acid sites are more intense than the peak corresponding to Bronsted and Lewis acid sites (1492cm^{-1}).

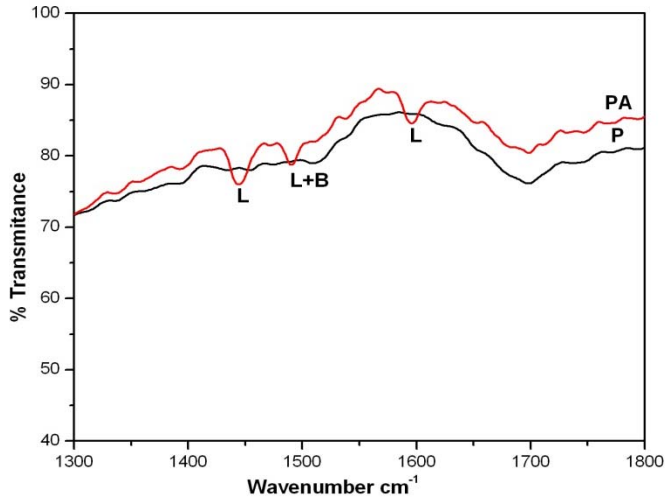
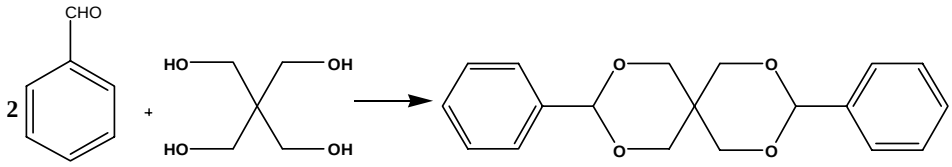


Fig. 3.7 FTIR spectra of pillared saponite (P) and the sample after adsorption of pyridine (PA).

3.2.3 Catalytic performance

A number of reactions were performed to find the activity of the catalyst; best activity was observed for the acetalation of pentaerithritol. Its importance was discussed in the beginning of this chapter. The reaction studied is shown in Scheme 1, in which benzaldehyde is taken as the example of carbonyl compound. Various factors which affect the acetal formation such as time, amount of catalyst, solvent were studied. The substrates considered in each case are those listed in Table 3.4, in which the yield obtained for each reaction is also given.



Scheme 1 Reaction of a carbonyl, benzaldehyde is taken as example and pentaerithritol to form the corresponding diacetal.

3.2.3.1 Effect of catalyst concentration on acetal formation

Effect of catalyst loading on product yield was studied at refluxing temperature over the catalyst for 2h. The catalyst concentration was varied from 1% to 3% taking benzaldehyde as carbonyl compound with mole ratio 2:1. The results are summarised in table 3.5. It is observed that the yield of the reaction was found to increase with increase in concentration of the catalyst up to 0.25 g. The optimum catalyst concentration of 0.25g was selected. Further increase in the amount of catalyst has no effect on the product formation, this may be due to the complete adsorption of active sites of the catalyst by reactants. The low yield at lower catalyst concentration may be due to the less adsorption of benzaldehyde on catalyst surface at lower catalyst concentration.

Table 3.5 Influence of amount of catalyst

Amount of catalyst	0.1g	0.15g	0.2g	0.25g	0.3
Yield (%)	68	72	86	93	93

3.2.3.2 Effect of substrate structure on acetal formation

Effect of various aldehydes and ketones was tested at optimised conditions over 0.25g of pillared saponite clay catalyst in toluene at refluxing temperature with 2,2-bis(hydroxymethyl)propane-1,3-diol. Aldehydes generally undergo nucleophilic addition more readily than ketones. For e.g. Dibenzalpentaerithritol was obtained in quantitative yield of 93% from refluxing toluene for 2h, where as bezophenone gave 24% from refluxing toluene for 8h. Bulkier aldehydes like veratraldehyde did not give any product, this may be due to diffusion problems.

3.2.3.3 Structure optimization by Computational methods

To know the exact structure of acetal formed in the reaction, structure optimization studies were conducted using DFT, B3LYP/6-311G (d, p) basis set, using Guassian 03 package. The optimised structure is shown in Fig.3.8. The ring system of the acetal forms a spirane like structure in different planes.

Optimised structure of acetal

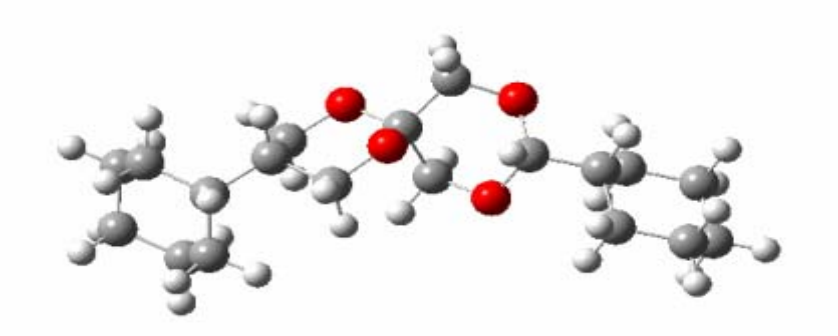
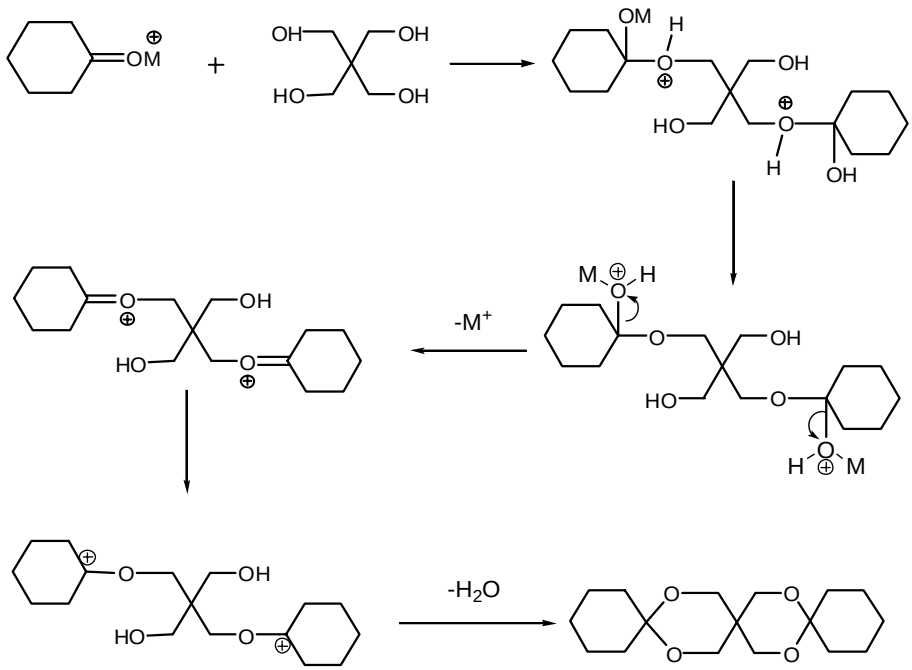


Fig.3.8 Optimised by B3LYP/6-311G (2d p)

3.2.3.4 Mechanism of acetal formation reaction

Acetal formation is believed to proceed through hemiacetal intermediates (Scheme 2) [83]. The carbonyl compound is first protonated by the Bronsted acid sites of the pillared clay catalysts, which provide enough space to diffuse in the interlayer and successive protonation to produce intermediates which combine with hydroxyl group to form the hemiacetal; protonation and subsequent dehydration gives the corresponding acetal. The rate determining step of acetalation is the formation of cation from the protonated hemiacetal. The bulkiness of hemiacetals might prevent the attack of the second hydroxyl group thereby changing the rate determining step. Another factor, the electron withdrawing power of phenyl group in these compounds, reduces the easy release of the pair of electrons on the carbonyl carbon during the reaction.



Scheme 2 Proposed Mechanism for the acetal formation.

Table 3.6 Preparation of diacetals from various carbonyl compounds catalyzed by pillared saponite

Entry	Substrate	Time (h)	Yield (%)[a]	Melting point (°C)	
				Found	Reported
1	Benzaldehyde	2	93	156	156
2	4-methyl benzaldehyde	4	74	183	-
3	2-nitro benzaldehyde	5	72	163	163
4	3-nitro benzaldehyde	3	78	71-72	72-73
5	4-methoxy benzaldehyde	3	68	155	155
6	4-hydroxy benzaldehyde	2	82	170	171
7	4-chloro benzaldehyde	3	84	141	141
8	4-bromo benzaldehyde	4	82	213	-
9	Veratraldehyde	8	-	-	-
10	Cyclopentanone	3	86	137	-
11	Cyclohexanone	3	90	116	116
12	4-tert butyl cyclohexanone	3	82	182	183
13	Benzophenone	8	24	162	164
14	Acetophenone	5	63	149	147

Reaction conditions: 2 mmol aldehyde, 1mmol pentaerithritol, 250 mg catalyst, 20ml toluene.
[a]Yield refers to isolated pure products

From the results presented in Table 3.6, it is evident that, in general, aldehydes undergo nucleophilic addition more readily than ketones. The formation of acetals using pillared clays as catalysts can be explained by two factors, diffusion properties of the substrates and electronic factors. As pointed out by Corma *et al*. [84], diffusion properties of ketones are the deciding factors rather than electronic factors. The bigger pore size of pillared clays promotes the rate of diffusion of the bulky products through the channels resulting in higher yields as compared to zeolites. The yield of the products correlates well with the expected electronic effects between the reactants and also with the polarity of C=O carbonyl group. Conversion of veratraldehyde was studied in order to analyse the influence of electronic and steric effects in the yield of the reaction. In this case, the oxonium ion formed in the third step is stabilized by the presence of methoxy groups in the 3, 5-positions. This is further supported by the fact that the carbonyl group may be completely blocked (steric effect) and no reaction occurs, which clearly illustrates the importance of the accessibility of the reactive groups of the reactants. This fact is supported by the results of Thomas *et al*. [85], who by their molecular docking simulation studies of cyclohexanone, acetophenone and benzophenone has pointed out that, as the size of the ketone increases, the acetalation efficiency has decreased. No acetal formation was observed during blank run, without the catalyst. The effect of aluminium pillaring on acetal formation was studied by comparing the results of natural saponite, three substrates were selected for this purpose. The corresponding yields obtained for benzaldehyde, cyclohexanone and 4-methyl benzaldehyde at optimised condition are 82.2%, 78.6% and 79.1%. These results confirm that pillaring favours the formation of acetals. The reason for this increase in yield after pillaring may be explained as, the formation of acetal is proceeding through a bulky intermediate, the increase in $d_{(001)}$ spacing upon pillaring can accommodate these intermediates leading to the product formation.

Between the aldehydes considered, it can be observed that the conversion increased following the order ortho- < meta- < para-substituted compounds, and between the para-substituted compounds, the influence of the nature of the substituent in the conversion varied as methoxy < hydroxy = bromo < chloro.

Finally, the recyclability of the catalyst was considered, and the catalyst was found to be stable over three cycles without appreciable loss in activity (table 3.7).

Table 3.7 Effect of recycling of catalysts

Entry	No. of recycling steps	% Yield [a, b]
1	1	93
2	2	88
3	3	82

[a] Reaction conditions: Benzaldehyde (2mmol), pentaerithritol(1mmol), 250mg Catalyst, toluene (20ml), Refluxing temperature.
[b] Yield refers to that of isolated pure products

3.2.3.5 Conclusion

Saponite was successfully pillared using aluminium polyoxocations, the catalyst was completely characterised using different analytical techniques. The pillared saponite was found to be an active, recyclable, thermally stable catalyst for the synthesis of cyclic acetals. Various factors affecting the catalytic activity like amount of catalyst, time etc was studied. The catalyst was recycled and reused without considerable loss in activity for three cycles.

3.3 Experimental

3.3.1 Purification of raw clay and preparation of the catalyst

The natural clay mineral used in this work was a saponite from Cabañas (Toledo, Spain), supplied by TOLSA (Madrid, Spain). The raw material was previously purified by dispersion-decantation, obtaining the 2 μm fraction [86].

The parent clay was intercalated with aluminium polycations, $[Al_{13}O_4(OH)_{24}(H_2O)_{12}]_{12}^{7+}$, in short Al_{13}^{7+}, according to a procedure described previously [87,88]. An aluminium polycation solution was prepared by slow addition of a solution of NaOH to a 0.1M solution of $AlCl_3 \cdot 6H_2O$, under vigorous stirring, with a mole ratio OH^-/Al^{3+} equal to 2.2. The resulting solution was left to aging for 24 h at room temperature under constant agitation. The solution was added to a previously prepared clay suspension at a ratio Al^{3+}: clay (1:5 mmol/g). The slurry was stirred for 24 h at room temperature, centrifuged and washed by dialysis with distilled water, dried in air at 70ºC for 16 h and calcined at 500 ºC for 2 h, at a heating rate of 5 ºC/min, in order to obtain the alumina-pillared saponite. The sample thus synthesized, pillared saponite, and was designated as Al-PILC.

3.3.2 Characterization techniques

X-ray diffraction (XRD) patterns of non-oriented powder samples, between 2º and 65º of 2θ with a scanning velocity of 2º/min, were obtained on a Siemens D-500 diffractometer with Ni-filtered Cu K α radiation, at 40 kV and 30 mA at SAIF, CUSAT.

Elemental analysis of the solids was carried out by inductively coupled plasma atomic emission spectroscopy (ICPS AES) at SAIF, CUSAT.

Nitrogen adsorption experiments were performed at –196 ºC on a static volumetric apparatus (Micromeritics ASAP 2010 adsorption analyzer). The samples, 0.2 g, were previously degassed at room temperature for 6 h and then for 2 h at 110 ºC at a pressure lower than 0.133 Pa. The specific total surface area (S_{BET}) was calculated using the BET equation from adsorption data in the relative pressure range between 0.05 and 0.20, and the micropore volume was obtained by means of the *t*-method [81].

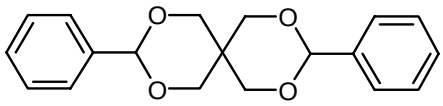
3.3.3 Catalytic performance

Acetalation of pentaerythirtol was carried out in a 50 cm^3 two necked glass batch reactor connected to a Dean-Stark apparatus. The reaction was carried out under nitrogen atmosphere. Solutions of pentaerithritol (1 mmol), aldehyde or ketone (3 mmol) in 20 cm^3 of toluene and 0.25 g of catalyst were stirred and refluxed. The progress of the reaction was monitored by thin layer chromatography on silica gel coated plates (Merck 60 F-254) using hexane:ethyl acetate mixture (10:2 v/v). After completion of the reaction, the products were obtained by evaporating the solvent in a rotary flash evaporator and subsequent recrystallization from ethanol gave the corresponding products.

All the reagents and solvents were of analytical grade or were purified by standard procedures prior to use. The products were characterized by FT-IR, NMR spectral methods. FT-IR spectra are recorded by the KBr pellet method on a JASCO FT-IR spectrophotometer in the range of 400 to 4000 cm^{-1}. ^1H NMR spectra were recorded on a Bruker 400 MHz instrument with tetramethylsilane (TMS) as internal standard in $CDCl_3$.

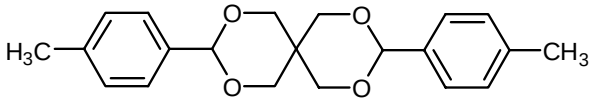
3.3.4 Characterisation of the products

Entry 1



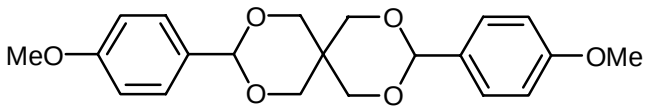
FT IR (KBr Vmax(cm^{-1})) 2918, 2856, 1577, 1383
^1H NMR ($CDCl_3$, 400MHz): 7.1-7.8 (m, 10H, Ar-H), 3.56 (d, 2H, J=11.4Hz), 3.86(d, 4H,J=11.4Hz) , 5.63 (s, 2H)

Entry 2



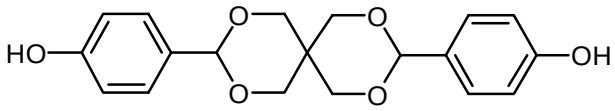
FT IR (KBr Vmax(cm^{-1})). 2923, 2863, 1610, 1455, 1395
^1H NMR ($CDCl_3$, 400MHz): 7.37(d, 4H, J=8.0Hz), 7.18(d, 4H, J=8.0 Hz)
5.43 (s, 2H) 4.58(d, 2H, J=11.6Hz), 3.73-38(m, 4H), 3.63(d, 2H, J=11.4Hz) 2.34(s, 3H)

Entry 4



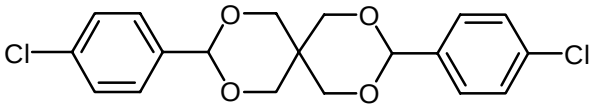
FT IR (KBr Vmax(cm^{-1}).2836, 1674, 1389, 1450, 1395 ^{1}H NMR ($CDCl_3$, 400MHz): δ (ppm) 7.42-6.96 (m, 8H), 5.82(s, 2H), 3.42(d, 2H J=11.1Hz) 3.83-3.87 (m, 4H), 3.96(d, 2H), 6.7-7.2(m, 8H), 5.80 (s, 2H), 3.6-3.8(m, 8H), 3.79(s, 6H)

Entry 5



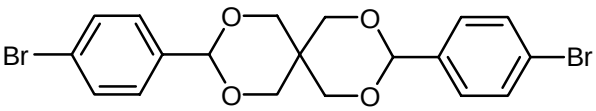
FT IR (KBr Vmax(cm^{-1}) 3465, 2865, 1605,1495,1060,780
^{1}H NMR ($CDCl_3$, 400MHz): δ (ppm) 7.56(br, s, 2H), 6.87-7.28 (m, 8H), 5.65(s, 2H), 4.84(d, 2H J=11.8Hz), 3.87-3.93(m,4H),3.70(d,2H, J=11.8Hz)

Entry 6



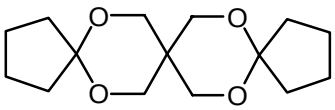
FT IR (KBr Vmax(cm^{-1}) 2990, 2856, 1577, 1240
^{1}H NMR ($CDCl_3$, 400MHz): δ (ppm) 7.30-7.50 (m, 8H), 5.43 (s, 2H), 4.829 (d, 2H, J=11.4Hz) 3.84(d, 4H, J=11.4Hz), 3.65(d, 2H, J=11.4Hz).

Entry 7



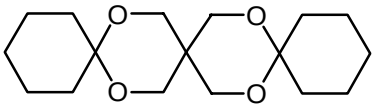
FT IR (KBr Vmax(cm^{-1}). 2976, 1558, 1264
^{1}H NMR ($CDCl_3$, 400MHz): δ (ppm) 7.23-7.38(m, 8H), 5.92 (s, 2H), 3.94-3.73(m, 4H), 3.71(d, 2H J=11.6Hz), 3.68(d, 2H J=11.6Hz)

Entry 9



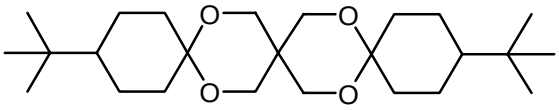
FT IR (KBr Vmax(cm^{-1}). 2994, 1495, 1250, 1120,780
^{1}H NMR ($CDCl_3$, 400MHz): δ (ppm) 3.72 (s, 8H), 2.15(m, 1H) 1.57-1.81(m, 16H)

Entry 10



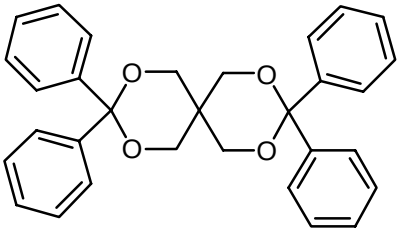
FT IR (KBr Vmax(cm^{-1}) 2892, 1550, 1115, 765
^{1}H NMR ($CDCl_3$, 400MHz): δ (ppm) 3.72 (s, 8H), 1.44-1.70 (m, 20H),

Entry 12



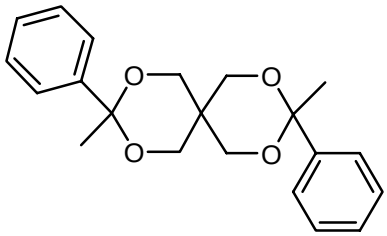
FT IR (KBr Vmax(cm^{-1}) 3010, 1610, 1242, 790
^{1}H NMR ($CDCl_3$, 400MHz): δ (ppm) 3.69(s, 8H) 1.27-1.75(m, 18H), 1.21 (s, 18 H)

Entry 13



FT IR (KBr Vmax(cm^{-1}) 2987, 1550, 1395, 1260
^{1}H NMR ($CDCl_3$, 400MHz): δ (ppm) 7.21(s, 20H) 3.62(m, 8 H)

Entry 14



FT IR (KBr Vmax (cm^{-1}) 2967, 1490, 1367, 1268
^{1}H NMR ($CDCl_3$, 400MHz): δ (ppm) 7.23(s, 10H) 4.56 (d, 2 H, J=11.4Hz), 3.84-3.72(m, 4H), 3.64(d, 2H, J=11.4Hz), 1.92(s, 3H)

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Chapter 4

CLAY SUPPORTED TRANSITION METAL BIMETALLIC CATALYST FOR HECK – COUPLING AND SUZUKI COUPLING REACTION

Contents

Bimetallic catalysts are more active than monometallic catalysts. Heterogeneous versions of common Pd catalysts have shown a number of limitations in use and have lengthy preparation procedures. In this chapter, preparation of clay supported Pd catalyst by simple ion exchange method, characterization of Cu-Pd, and Co-Pd bimetallic catalysts and their application in Heck coupling and Suzuki coupling reactions are presented.

4.1 Introduction

Bimetallic catalysts have been proved to be important materials for many catalytic applications [1–4] and are well known for exhibiting properties that are distinctly different from those of the corresponding monometallic catalysts [2, 5]. Many investigations combining experimental studies and theoretical calculations have been performed with the goal of correlating electronic properties of bimetallic surfaces with reaction pathways [6–11]. It has been demonstrated that bimetallic surfaces also play a significant role in controlling their electronic

and catalytic properties [12-14]. Kitchin et.al. have shown that, for Ni/Pt (III) bimetallic surfaces with a Ni coverage at one monolayer (ML), Ni atoms can reside either on the surface to produce a Ni-terminated Ni–Pt(111) surface or in the subsurface region to form a Pt terminated Pt–Ni–Pt (111) sub surface structure. The ML Pt–Ni–Pt (111) structure is characterized by unique chemical properties that are distinctively different from Pt (111), Ni (111), or the surface Ni–Pt–Pt (111) structure [15-17].

Jiang, et al [18] reported that Ru-Cu bimetallic catalyst supported on clay with the aid of ionic liquid effectively catalyse the hydrogenolysis of glycerol. Al-pillared clay supported Cu-Pd catalyst by wet impregnation method was reported to be active for the nitrate reduction [19]. Noble metals (Pd and Pt) in combination with various promoters such as Cu [20–24], Sn [25], In [26], Ag and Au [27] dispersed on solid supports are highly active for nitrate conversion. The role of promoters in this catalyst system is to reduce the formation of byproducts such as nitrites and ammonia with simultaneous increase in the catalytic activity. Pd-Cu bimetallic particles supported on ceria [28], alumina [29], titania [30] and polypyrrole [31] have been found to have considerably higher catalytic activity compared to monometallic Pd catalyst. Allylation of aldehydes using Mg-Cd bimetallic catalyst was reported by Venkat et al [32]. Carbon-supported bimetallic catalysts containing iron with various other metals such as Co, Ni etc were found to be effective catalyts for benzene hydrogenation and thiophene hydrodesulphurization [33].

The palladium catalysed vinylation of aryl halides provides a very convenient and powerful method for forming carbon-carbon bonds at unsubstituted vinylic positions [34]. Major improvements in Heck-type reactions over the last decade have been brought about by the introduction of tetraalkyl ammonium salts, silver (I) or thallium (I) salts as promising additives or by use of organo trifluromethane sulphonate [35]. Two recent

promising approaches involve reactions in aqueous (or water-organic solvent) media [36] and the use of vinyl iodonium salts [37]. For Heck reaction, a Pd (II) salt or complex is employed which is reduced *in situ* to an active zero valent palladium species under homogeneous conditions. The Pd (II) species that is subsequently regenerated in the reaction is very difficult to separate from the reaction mixture and reuse for the reaction directly without further processing. In view of the practical and industrial applications, improvements in catalyst efficiency and catalyst recycling are essential. To overcome these problems, heterogeneous catalysts such as polymer-supported palladium catalysts and Pd-Ph_2P-Si supported on clay have been reported for the arylation of alkenes [38], Suzuki cross-coupling reaction catalyzed by cyclopalladated complexes of tertiary amines immobilized on ionic liquid $[Bmim]^+$ $BF4^-$ was reported [39]. However, these catalysts suffer from drawbacks such as (i) their preparation involves many steps and use of expensive phosphorus and silicon compounds and (ii) deactivation of the catalyst on its reuse. There are a number of supported catalysts reported recently by heterogenization of homogeneous catalysts for Suzuki and Heck coupling reaction such as palladium complex immobilized on polymer support [40-41] or inorganic support [42].

4.2 Results and discussion

Clay KSF supported bimetallic catalysts were prepared by exchanging clay with dilute solutions of Pd $(CH_3COO)_2$ and $Cu(NO_3)_2$. The catalysts prepared were characterized by various physicochemical methods. The metal content of the catalysts was estimated using electron disperse X-ray microscope (EDX) connected to a JOEL microscope. The results are shown in table 4.2, the presence of copper and palladium are confirmed from the EDX. The metal content in the catalysts was determined by ICP AES. The values are given in table 4.1.

Table 4.1 ICP AES result of catalysts

	Na	Mg	Al	Si	K	Ca	Fe	Cu	Pd
KSF	2.2	2.8	18.8	58.2	4.2	2.9	11.5	0	0
Cu-Pd KSF	0.9	1.4	12.8	54.6	3.8	1.6	10.6	0.81	1.8

Table 4.2 EDX Data of KSF Pd-Cu

Element	(keV)	Mass%	Atom%	K
C K	0.277	13.07	21.32	2.62
O K	0.525	36.32	44.48	1
Mg K	1.253	1.47	1.18	0.72
Al K	1.486	19.77	14.36	0.75
Si K	1.739	22.01	15.36	0.76
K K	3.312	5.68	2.85	1.13
Fe K	6.398	0.66	0.23	2.35
Cu K	8.04	0.27	0.08	3.73
Pd L	2.838	0.75	0.14	3.34
Total		100	100	

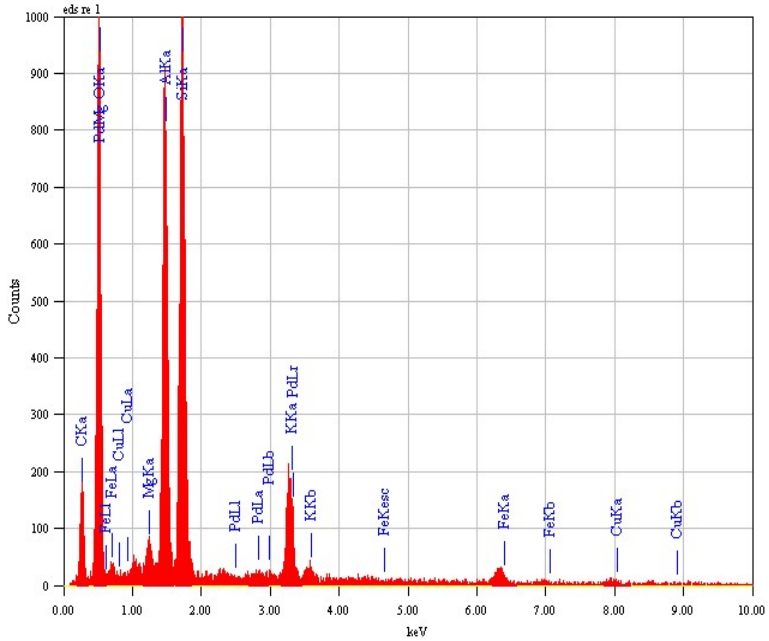


Fig. 4.1 EDX spectra of KSF Pd-Cu

SEM analysis of the KSF Pd-Cu catalyst showed that the flake like structure of the montmorillonite KSF was maintained upon modification. Fig.4.2 depicts the SEM micrograph of KSF Pd-Cu catalyst.

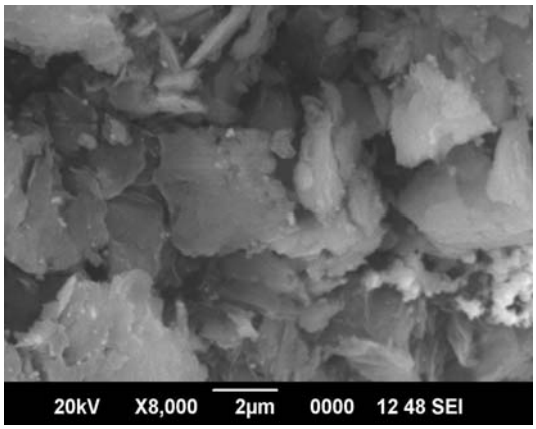


Fig. 4.2 SEM image of the KSF Pd-Cu

FT IR spectra of the catalyst showed that, all the peaks present in the parent clay were maintained in the modified catalyst except a decrease in intensity of the peak corresponding to SiO_4 tetrahedra centered around 1000 cm^{-1} (fig 4.3).

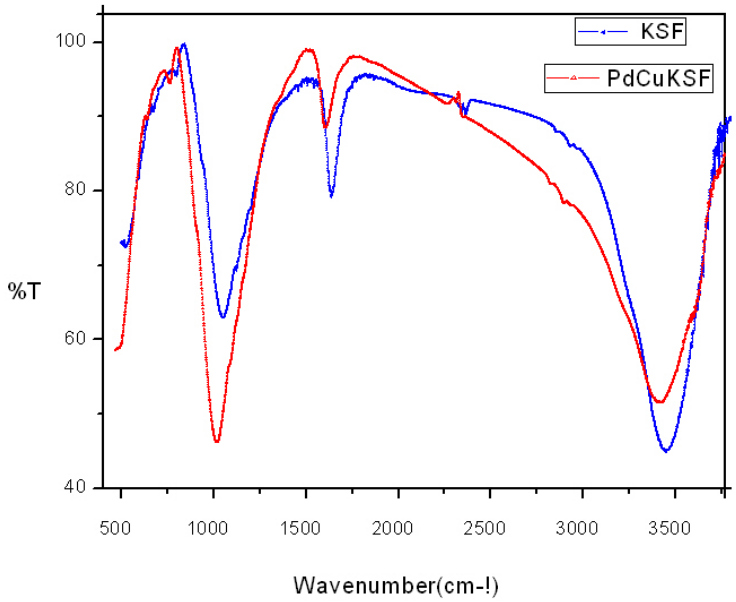


Fig. 4.3 FTIR spectra of KSF and KSF Pd-Cu

Thermal stability of the catalyst was studied by TG analysis. The TG plots of the KSF Pd-Cu (fig.4.4) showed a weight loss around 100°C, due to loss of physically adsorbed water. Water loss in this temperature range is an indication for non crystalline hydrated water. Thermogravimetric analysis shows that the catalyst was stable up to 800°C.

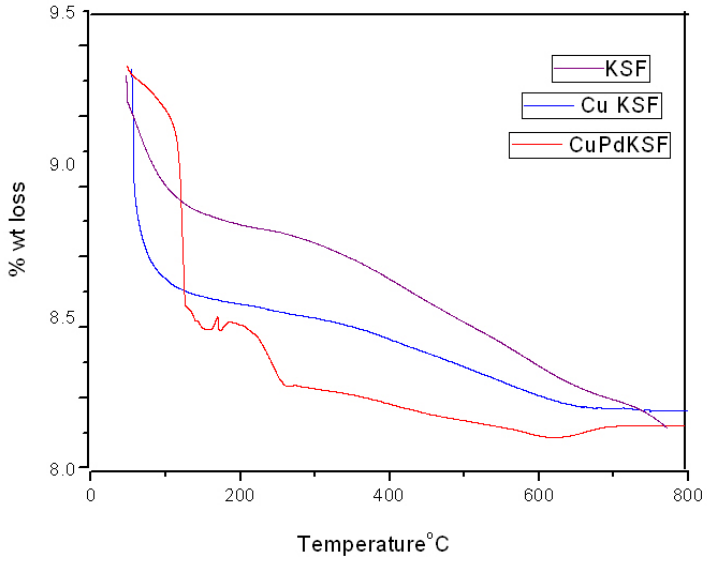


Fig. 4.4 Thermogravimetric plot of catalysts

Definite information about the nature of the metals present in the catalyst could be obtained from cyclic voltametry(CV). Fig 4.5 shows the CV of Pd-Cu exchanged Montmorillonite KSF at a scan rate of 50mVs^{-1}. It clearly indicates two reversible peaks with $E_{1/2}$(vs saturated calomel electrode) at -0.119V and +0.117V. The peak at +0.117V may be assigned to a Pd/ Pd^{2+} process and one at -0.119V to a Cu^{2+}/Cu process. Two one-step electron processes (i.e. Cu^{2+} /Cu^{+} and Cu^{+}/Cu) are possible [43]. Hence the presence of Pd is mediating the Cu^{2+}/Cu redox process (Fig.4.6). This explains the high activity of the KSF Pd-Cu exchanged catalyst compared to Cu or Pd exchanged catalyst, this was confirmed by the results obtained for the Heck coupling reaction with catalysts containing various amounts of the metals (Table 4.3)

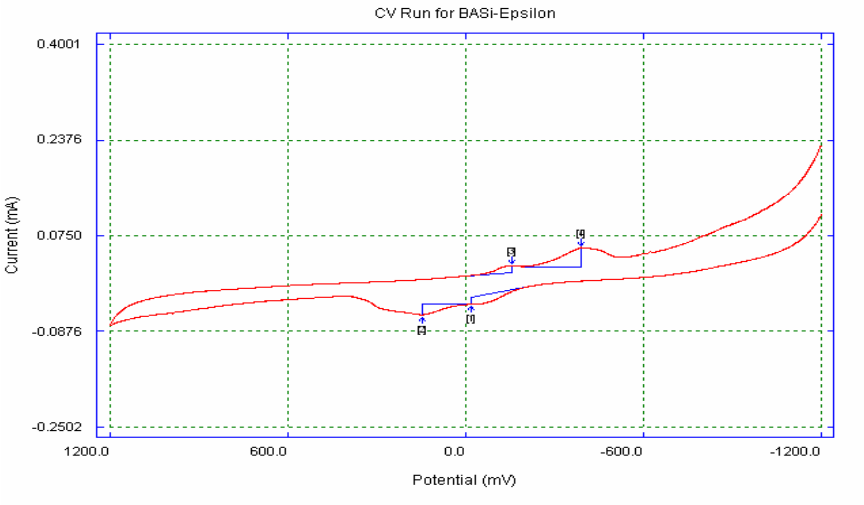


Fig. 4.5 Cyclic voltammogram of KSF Pd-Cu

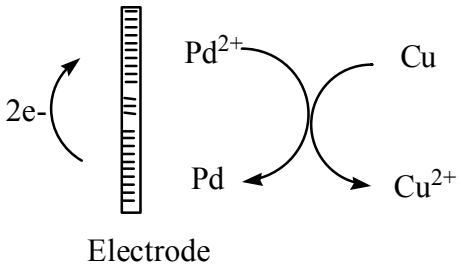


Fig. 4.6 Pd mediates the redox behavior of Cu

Surface area of the copper exchanged KSF and Pd-Cu exchanged catalysts are shown in table 4.3. The surface area of the catalyst is increased upon metal exchange.

Table 4.3 Surface area of the catalysts

Catalyst	Suface area(m^2/g)
KSF	15.00
Cu KSF	72.23
Cu Pd KSF	155.0

UV-DRS spectra of the prepared catalyst show an absorption band around 430nm corresponding to the d-d transition of copper present in the catalyst system (Fig.4.7).

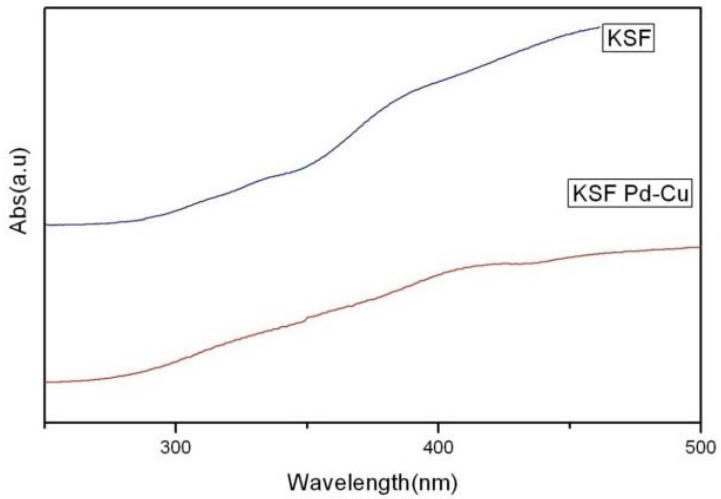
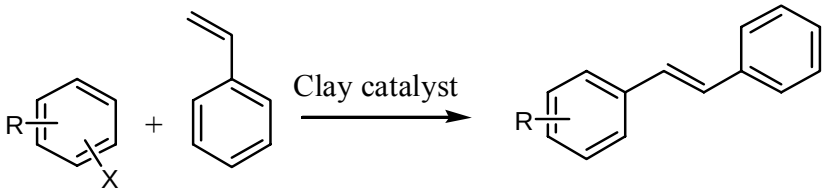


Fig. 4.7 UV-DRS spectra of CuPd KSF

4.2.1 Heck Coupling Reaction



Scheme 1 Heck coupling reaction

The Heck coupling reaction was carried out with various catalysts, the results are shown in Table 4.4 Using the catalyst with copper alone at 1 wt %, the yield was very low, as the concentration of copper was increased, the yield of the product also increased to 25%. When Pd-Cu was employed for the reaction, the yield was increased to 72 % which clearly indicated the role of bimetallic catalyst in the reaction. The higher activity of this catalyst seems to be due to a synergistic effect produced by the presence of Pd and Cu in close vicinity. The results also indicate that, for this catalyst to be more active, 2.5 wt % of copper must be present along with palladium.

Table 4.4 Heck coupling reaction using various catalysts

Entry	Catalyst	Yield %
1	Cu(1 wt%)-KSF	10
2	Cu (2.7 wt%)-KSF	25
3	Cu (2.5 wt %)-Pd (7.5wt%)-KSF	72
4	Co(1 wt %) -KSF	0
5	Co(3 wt %)-Pd(6 wt%)-KSF	48

Reaction conditions: Iodobenzene (3 mmol), Styrene (6 mmol), anhy K_2CO_3(8 mmol), 100 mg catalyst, Solvent: THF 5ml, Reflux temperature

Effect of solvent was studied by selecting five different solvents, the reaction proceeded well in polar solvents as compared to non polar solvents (table 4.5). Maximum yield was obtained for DMF and was selected as the solvent of choice.

Table 4.5 Influence of solvent on Heck-Coupling reaction

Entry	Solvent	% Yield
1	Toluene	52
2	Ethanol	55
3	Acetone	55
4	DMF	67
5	THF	62

Reaction conditions: Iodobenzene (3 mmol), Styrene (6 mmol), anhy K_2CO_3 (8 mmol), 100 mg catalyst, Solvent 5ml, Reflux temperature

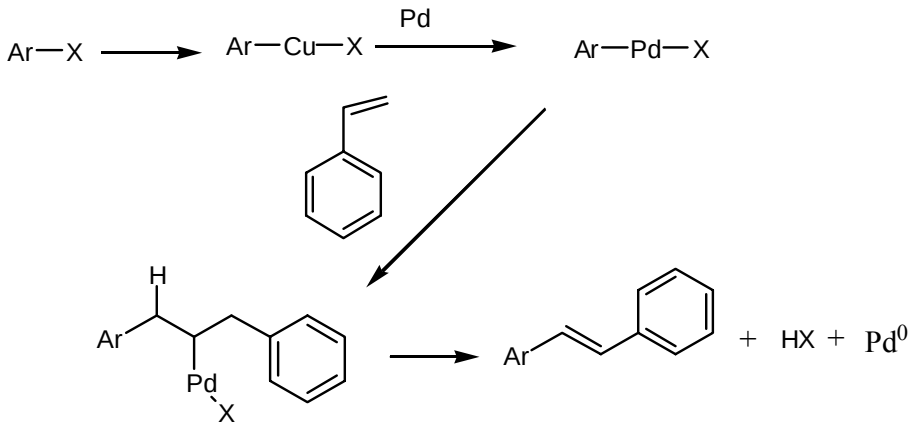
The usefulness of KSF Pd-Cu as catalyst was studied by taking various substrates, remarkable feature of this catalyst system was that, even less reactive, substituted bromobenzenes reacted with styrene to give (E)-Stilbenes. Different bases such as K_2CO_3, Et_3N and NaOH were studied; good result was obtained with K_2CO_3; results are summarized in table 4.6.

Table 4.6 Heck Coupling reaction with various substrates

Entry	R	X	Base	t/h	Yield%
1	H	I	K_2CO_3	4	67
2	H	I	Et_3N	4	62
3	H	I	NaOH	4	64
4	CH_3	I	K_2CO_3	4	76
5	CH_3	I	Et_3N	4	74
6	CH_3	I	NaOH	4	73
4	H	Br	K_2CO_3	8	49
5	H	Br	Et_3N	8	43
6	H	Br	NaOH	8	46
7	H	NO_2	K_2CO_3	24	0
8	H	NO_2	Et_3N	24	0
9	H	NO_2	NaOH	24	0

Reaction condition: Reaction conditions: Aryl halide (3 mmol), Styrene (6 mmol), anhy K_2CO_3 (8 mmol), 100 mg catalyst, Solvent: DMF 5ml, Reflux temperature.

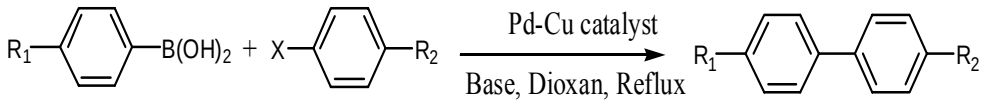
Mechanistically, it is proposed that aryl halides react with copper presumably to yield an organocopper species, which undergoes transmetallation with Pd (II) followed by olefin insertion, β-hydride elimination and finally dissociation of palladium hydride species [44-45].



Scheme 2 Proposed mechanism of Heck-Coupling reaction

4.2.2 Suzuki Coupling Reaction

The Suzuki cross-coupling reaction [46-47] is one of the most powerful methodologies for the generation of new carbon-carbon bonds, particularly in the synthesis of biaryls. The traditional Suzuki cross-coupling reaction, however, suffers from a number of drawbacks such as catalyst loss into the product, catalyst decomposition and poor reagent solubility. The activity of the CuPd KSF catalyst in Suzuki coupling reaction between benzene boronic acids and aryl halides was studied. The reaction is shown in Scheme 3



Scheme 3 Suzuki coupling reaction catalysed by KSF Pd-Cu

Effect of solvent was studied by selecting five different solvents at reflux temperature, good results were obtained for polar solvents as compared to non polar solvents. The increased activity in polar solvents in these reactions may be ascribed to the smooth interaction of the substrates on the active sites of the catalyst due to easier diffusion effect of polar solvents as compared to non polar solvents. The results are summarized in table 4.7

Table 4.7 Effect of solvent on Suzuki Coupling reaction

Entry	Solvent	% Yield
1	Toluene	78
2	Methanol	43
3	Dioxan	87
4	THF	72
5	Acetone	69

Reaction condition: 4-nitro iodobenzene (1 mmol), benzene boronic acid (1.2 mmol), K_2CO_3 (3 mmol), Reflux temperature. 5 mL solvent

Different substrates were tried, aryl iodides and bromides gave good results while chlorides gave poor yield even after prolonged reaction under refluxing conditions. The results are summarized in table 4.8. The electronic factors of substrates had no considerable effect on the reaction, but steric effect had considerable influence. When bulkier substituents were present (like tertiary butyl groups), the yield was decreased. This may be due to slow or hindered diffusion of the substrates to access the catalyst active sites due to the hindrance offered by the layered structure of the catalyst.

Table 4.8 Suzuki Coupling reaction of various substrates

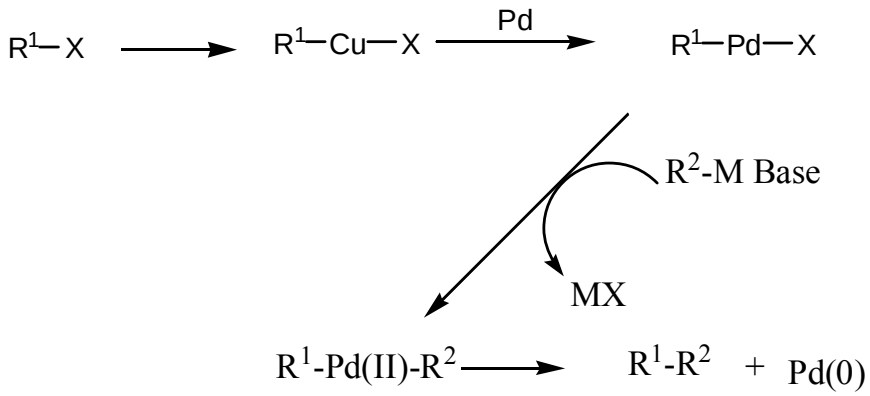
Entry	R1	R2	X	Base	% Yield
1	H	CH_3	I	K_2CO_3	86
2	H	CH_3	I	Et_3N	82
3	H	CH_3	I	NaOH	85
4	H	H	I	K_2CO_3	79
5	H	H	I	Et_3N	71
6	H	H	I	NaOH	76
7	H	H	Cl	K_2CO_3	24
8	H	NO_2	I	K_2CO_3	87
9	H	NO_2	I	Et_3N	81
10	H	NO_2	I	NaOH	84
11	H	$C(CH_3)_2$	I	K_2CO_3	69
12	H	-$COCH_3$	Br	K_2CO_3	76

Reaction condition: aryl halide (1 mmol), benzene boronic acid (1.2 mmol), Na_2CO_3 (3 mmol), 100 mg catalyst Solvent: 5ml dioxan at 100^oC, Reaction time: 24h. Isolated yield

4.2.2.1 Reaction mechanism

By analogy to the other cross coupling reactions, the catalytic cycle of Suzuki coupling reaction involves three basic steps: 1) Oxidative addition, 2)

Transmetallation and 3) Reductive elimination [48]. The mechanism of CuPd KSF catalysed Suzuki Coupling reaction is shown in scheme 4. The aryl halide reacts with copper present in the catalyst giving aryl copper halide in the first step which upon transmetallation gave aryl palladium halide. The efficiency of palladium originates from its ability, when it is zero valent, to activate C-X bonds (X=I, Cl, Br, O) by an oxidative addition which provides an organopalladium (II) complex which is prone to react with nucleophiles [49,50]. Oxidative addition of 1-alkenyl, 1-alkynyl, allyl, benzyl and aryl halides to a Pd(0) complex gives a stable trans palladium (II) complex [51]. The oxidative addition followed by reductive elimination gives the product. The reaction proceeds with complete retention of stereochemistry for alkenyl halide and with inversion for allylic and benzylic halides. Oxidative addition is often the rate limiting step in the catalytic cycle [52] (Scheme 4).



Scheme 4 Mechanism of KSF Pd-Cu catalysed Suzuki Coupling reaction

The catalyst was recycled by washing with acetone, methanol and ethyl acetate followed by drying at room temperature under vacuum. The catalyst was used four times without appreciable loss in activity.

Table 4.9 Recycling studies

Entry	No. of recycling steps	% Yield
1	1	87
2	2	85
3	3	82
4	4	80

Reaction condition: 4-nitro iodobenzene (1 mmol), benzene boronic acid (1.2 mmol), K_2CO_3 (3 mmol), 100mg catalyst 5ml dioxan at 100 ^oC. Reaction time 24h. Isolated yield

4.3 Conclusions

- KSF Pd-Cu bimetallic catalyst was prepared and characterized
- The catalyst was found to be active for Heck and Suzuki coupling reaction
- The catalyst was found to be active over four cycles

4.4 Experimental

4.4.1 Preparation of catalysts

The copper exchanged montmorillonite KSF was prepared by stirring 3 g of activated clay with 30 mg and 81 mg $Cu(NO_3)_2$ in water (50 ml) over night, filtered washed with water extensively until the filtrate was free from NO_3^- ions. It was dried at 150^{o}C for 1h.

Palladium exchanged montmorillonite KSF was prepared by stirring 3 g of activated clay with 225 mg of $PdCl_2$ in water (50 ml) over night, filtered, washed with water (20ml x 5 times) and dried at 150^{o}C for 1h.

Pd-Cu exchanged montmorillonite KSF catalyst was prepared by stirring 3 g of activated clay with 80 mg of $Cu(NO_3)_2$ and 225 mg of $PdCl_2$ in water (50 ml) over night, filtered, washed with water (20ml x 5 times) and dried at 150^{o}C for 1h.

Cobalt exchanged montmorillonite KSF was prepared by stirring 3 g of activated clay with 30 mg of $CoCl_2$ in water (50 ml) overnight, filtered washed with water (20ml x 5 times) until the filtrate was free from Cl^- ions, and dried at 150°C for 1h

Pd-Co exchanged montmorillonite KSF was prepared by stirring 3g of activated clay with 90 mg of $CoCl_2$ and 180 mg of $PdCl_2$ in water (50 ml) overnight, filtered, washed with water (20ml x 5 times) until the filtrate was free from Cl^- ions, and dried at 150°C for 1h

4.4.2 General procedure for Heck coupling reaction

A 10 ml RB flask was charged with aryl halide (3mmol), styrene (6 mmol), anhy K_2CO_3 (8 mmol).The catalyst (100 mg) (KSF Pd-Cu) was added to it followed by DMF (5 ml). The reaction mixture was stirred at reflux temperature. The progress of the reaction was followed by TLC using hexane: ethyl acetate (8:2) .After completion of the reaction, the catalyst was separated by filtration and the reaction mixture was poured in to water followed by its extraction with ethyl acetate to give the crude product which was subsequently purified by column chromatography using Hexane: ethyl acetate(8:2) as eluent.

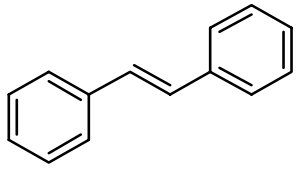
4.4.3 General procedure for Suzuki coupling reaction

A 10 ml RB flask was charged with aryl halide (1 mmol), aryl boronic acid (1.2 mmol), and K_2CO_3 (3 mmol). The catalyst KSF Pd-Cu (100 mg) was added to it followed by 5 ml of dioxan. The reaction mixture was stirred at reflux temperature. The progress of the reaction was monitored by TLC using hexane: ethyl acetate (10:1). After completion of the reaction, the catalyst was filtered and the catalyst was washed with acetone and with small portions of ethyl acetate several times. The combined washings were washed with water in a separating funnel, the organic layer was isolated and dried with 4A°

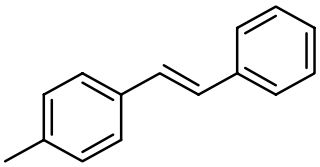
molecular sieves. The pure product was isolated by column chromatography using hexane: ethyl acetate (10:1) as eluent.

4.4.4 Characterisation of the products

4.4.4.1 Heck products (Stilbenes)



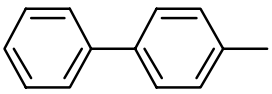
^{1}HNMR (400 MHz; $CDCl_3$):δ 6.99 (d, 2H J=2.4 Hz), 7.15(d, 2H, J=7.9Hz), 7.3(m, 1H), 7.35 (t, 2H, J=6.36Hz), 7.4(d, 2H J=8.12Hz), 7.5(d, 2H J=2Hz)



^{1}HNMR (400 MHz; $CDCl_3$): δ2.36(s, 3H), 7.03 (d, 2H J=2.6 Hz), 7.17(d, 2H, J=8.0Hz), 7.33(m, 1H), 7.36 (t, 2H, J=6.36Hz), 7.42(d, 2H J=8.1Hz), 7.51(d, 2H J=1.3Hz)

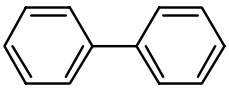
4.4.4.2 Suzuki products (Biphenyls)

4- Methylbiphenyl



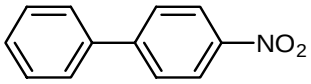
^{1}HNMR (400 MHz; $CDCl_3$): δ 2.4(s, 3H), 7.07(d, 2H, *J* = 7.3 Hz), 7.2- 7.3 (m, 1H), 7.35 (t, *J* = 2H, 6.36 Hz), 7.42 (d, 2H, *J* = 8.12), 7.48- 7.53 (m, 2H).

Biphenyl



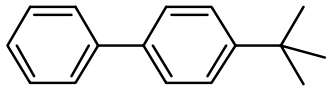
^{1}HNMR (400 MHz; $CDCl_3$): δ7.23-7.34 (m, 2H), 7.36-7.42 (m, 4H), 7.56-7.59 (m, 4H).

4- Nitrobiphenyl



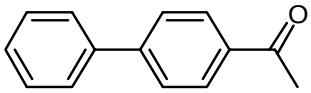
^{1}HNMR (400 MHz; $CDCl_3$): δ 7.37-7.41 (m, 1H), 7.43-7.45 (m, 2H), 7.57(m, 2H), 7.66 (d, 2H, *J* = 8.80 Hz), 8.29 (d, 2H, *J* = 8.80 Hz).

4- tertiary butylbiphenyl



^{1}HNMR (400 MHz; $CDCl_3$): δ 1.4 (s, 9H), 7.34-7.64 (m, 9H).

4- Acetylbiphenyl



^{1}HNMR (400 MHz: $CDCl_3$): δ 2.6 (s, 3H), 7.32-7.50(m, 3H), 7.60- 7.70 (m, 4H), 8.0 (d, 2H, *J* = 6.2 Hz).

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Chapter 5

CLAY SUPPORTED CHIRAL DIPEPTIDE METAL COMPLEX CATALYSTS: PREPARATION, CHARACTERIZATION AND APPLICATION IN AZA-DIELS ALDER REACTION

Contents

Development of new catalysts for enantiomerically pure compounds in organic synthesis is an important area of research. Heterogeneous versions of chiral catalysts are limited, inspite of a number of advantages. Peptides are cheaper sources of chiral inducing agents. In this chapter, preparation of clay supported dipeptide catalysts of Cu and Ti, characterization and application for the synthesis of Pyrano[3,2,c] and Furo[3,2,c] quinolines via Aza Diels Alder reaction are discussed in detail.

5.1 Introduction

Naturally occurring alkaloids play an important role in numerous areas of modern chemical industry, such as in medicine, cosmetics, agriculture and nutrition science. These compounds were often originally found in nature and have later prepared by synthetic methods.

The development of a method to synthesize optically active compounds has always received much attention in various areas of organic and biological chemistry [1]. Enantiomerically pure compound consists of only one of its mirror image isomers (enantiomers). There are numerous examples of structures where the two enantiomers express different biological activity in living organism. One such example, which highlights the importance of enantiomeric purity, is naproxen (Fig.5.1), where the (S)-enantiomer is the active ingredient in an anti-inflammatory drug, while the (R)-enantiomer is a liver toxin.

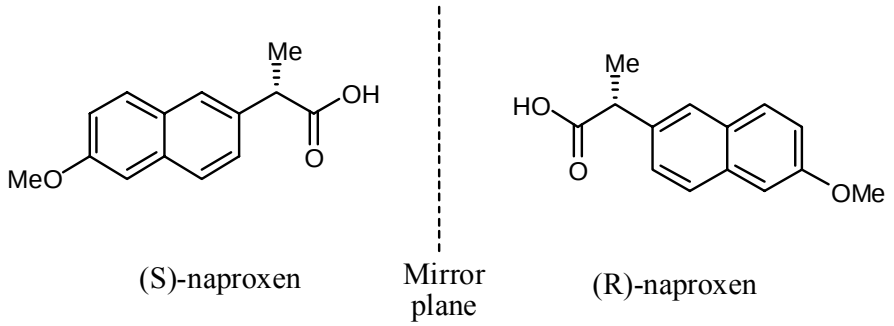


Fig.5.1 The enantiomers of naproxen show dramatic difference in biological activity.

Preparation of optically active compounds is important for drug development. Various strategies have been developed to prepare enantiomer enriched compounds and can be divided into three subgroups: resolution methods where a racemic mixture is separated; use of chiral pool thereby starting with a chiral substrate and asymmetric synthesis.

Different methodologies can be applied to induce stereoselectivity via asymmetric synthesis. One way is the attachment of a chiral auxiliary to the substrate that directs new transformations to give the desired stereoisomer. After the reaction, the chiral auxiliary is cleaved from the molecule. A drawback with this approach is the requirement of additional synthetic steps for attachment and cleavage of the auxiliary and the need for stoichiometric

amounts of the enantiomerically pure entity. Asymmetric catalysis is another opportunity that allows the use of substoichiometric amounts of chiral inductor such as chiral Lewis acids or an enzyme. This approach allows better atom efficiency, since, only a small amount of the catalyst is required in the catalytic cycle and this catalyst induces stereoselectivity.

5.1.1 Lewis acids in organic synthesis

In 1923 G.N. Lewis broadened the acid base theory considerably by proposing that acids could be defined as electron-pair acceptors and bases as electron pair donors [2]. The number of organic reactions like Friedel-Crafts-, ene, and Diels Alder reaction which make use of Lewis acids as catalysts such as $AlCl_3$, $TiCl_4$, $BF_3.OEt_2$ and $SnCl_4$ is still increasing. Choosing an appropriate Lewis acid is a delicate task and optimizations are generally required since many of them, especially chiral ones are substrate dependent. However supported Lewis acid catalysts in organic synthesis are limited.

5.1.2 Aza Diels Alder reaction

A useful method for the synthesis of six-membered rings is the Diels Alder reaction. The Aza-Diels Alder reaction provides a useful method for the incorporation of a nitrogen atom in the ring structure with the possibility to control regio, diastereo- and enantio-selectivity [3-5]. The hetero Diels Alder reaction of imines with dienes forming nitrogen-containing cycloadducts is therefore an important field of research [6, 7]. The reactivity of the imines can be increased by activating groups such as sulphonyls or carbonyls and are commonly used to promote imine reactivity in Diels-Alder reactions. These activating groups may be attached either to the imine carbon or the nitrogen atom or to both. MO calculations have suggested that carbonyl substituent are more activating than sulfonyl ones, with a more pronounced effect for electron withdrawing substituents bound to the imine carbon atom than those bound to

nitrogen [8]. A Diels-Alder reaction involving an azirine is shown in Fig 5.2 (a) by the reaction between 3-phenyl-2H-azirine and Danishefsky's diene. (b) The symmetry allowed Diels-Alder reaction can take place either by a normal electron-demand HOMO diene-controlled process (b) or through an inverse electron-demand LUMO diene-controlled reaction(c) [9].

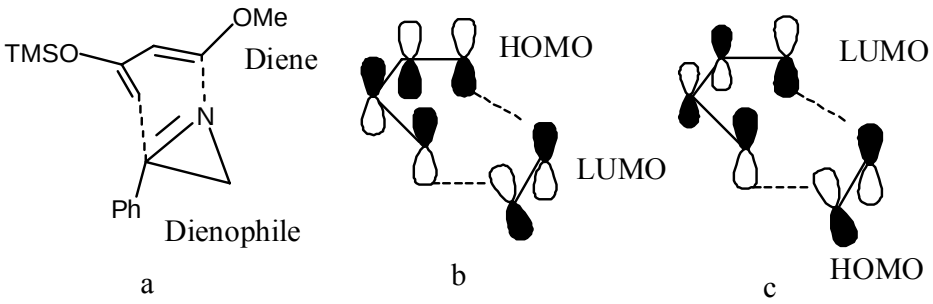


Fig.5.2 Basic concepts of Diels-Alder reaction

5.1.3 Aim of this study

The development of a method to synthesize optically active compounds has always received much attention in various areas of organic and biological chemistry [10]. The design of chiral metal complexes as catalysts for asymmetric organic reactions has been widely studied with the metal complex derivatives of binaphthol, tartaric acid and semicorrin [11-13]. In the area of organic synthesis, α-amino acids are one of the most frequently used sources of chirality. The use of both natural and unnatural α-amino acids and their derivatives as chiral reagent auxiliaries and ligands for asymmetric catalysis is wide - spread [14-16]. In contrast, peptides and their complexes have rarely been reported as effective ligands of metallic species in asymmetric reactions [17]. Peptide titanium complex was reported as catalyst for asymmetric hydrocyanation under homogeneous conditions [18-19]. The development of chiral lewis acid catalysts for carbon-carbon bond forming reactions is one of the most challenging formidable goals in organic synthesis [20]. The catalytic

asymmetric reaction with imine, can open a wide variety of possibilities for the synthesis of natural product of alkaloid family [21]. Generally these compounds are prepared by Aza-Diels Alder reactions of imines derived from aldehydes and amines with dihydropyran or dihydrofuran. Chiral lanthanide lewis acids [22], various transition metal complexes as catalysts were reported for the synthesis [23-25]. However there are very few reports on supported catalysts for asymmetric organic synthesis [26, 27]. In the present work, an attempt was made to prepare clay supported chiral dipeptide catalysts, revealing that peptide metal complex if effectively designed and supported on a cheap support, can be potentially useful chiral auxillaries because enzymes, natural peptides, exhibit remarkably high stereo specificities and stereoselectivity in biochemical reactions.

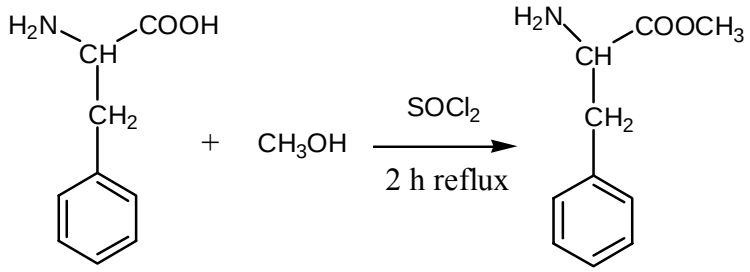
5.2 Results and Discussion

The peptides used were acyclic dipeptide esters whose amino terminal was modified to Schiff bases derived from naphthaldehyde or salicylaldehyde derivatives to facilitate complexation with metal ions [28]Titanium isopropoxide and $CuCl_2$ were used as metallic species. Synthesis of dipeptides bearing naphthaldehyde Schiff base were carried by a procedure described in the literature [29], which involved the coupling of an amino acid, whose amino group was modified to Schiff base by condensation with 2-hydroxy-1-naphthaldehyde, with another amino acid methyl ester by using dicyclohexylcarbodiimide (DCC) in dichloromethane

5.2.1 Preparation of L- Phenylalanine methyl ester

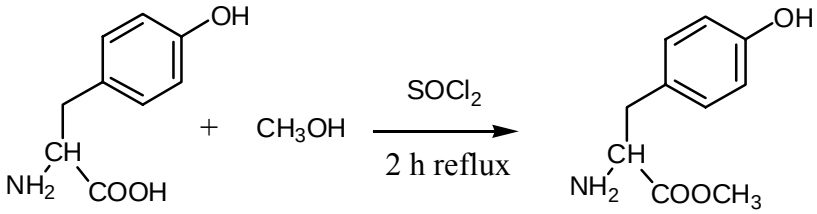
The carboxyl group of the amino acid was esterified with methanol in the presence of $SOCl_2$ .The product obtained was purified by recrystallisation. The synthesis of methyl esters of phenyl alanine and tyrosine are shown in scheme 5.1 and 5.2. The amino acid methyl esters were prepared reacting the L-amino acids with methanol in the presence of thionylchloride. Pure amino

acid methyl esters were obtained by fractional precipitation from methanol solution using dry ether.



Scheme 5.1 Preparation of Phenylalanine methyl ester

5.2.2 Preparation of Tyrosine methyl ester



Scheme 5.2 Preparation of Tyrosine methyl ester

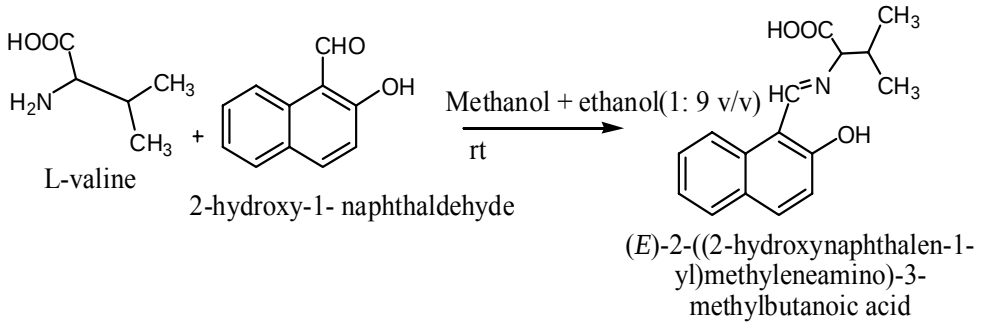
The excess thionyl chloride was distilled off under vacuum. The amino acid methyl ester was extracted with hot methanol and recrystallised and or fractionally precipitated from methanol.

5.2.3 Preparation of amino acid Schiff base

Schiffs bases are commonly used for the synthesis of metal complexes for various catalytic applications. Schiff base ligands are able to coordinate metals through imine nitrogen and another group, usually linked to the aldehyde. Modern chemists still prepare Schiff bases, and nowadays active and well-designed Schiff base ligands are considered ‘‘privileged ligands’’[30]. In fact, Schiff bases are able to stabilize many different metals in various oxidation states, controlling the performance of metals in

a large variety of useful catalytic transformations. Stereogenic centres or other elements of chirality (planes, axes) can be introduced in the synthetic design.

The Schiff bases of amino acids were synthesized by reacting equimolar mixture of amino acid and 2-hydroxy-1-naphthaldehyde in a mixture of ethanol and methanol. The product obtained was washed with diethyl ether to give the corresponding amino acid Schiff base (Scheme 5.3).

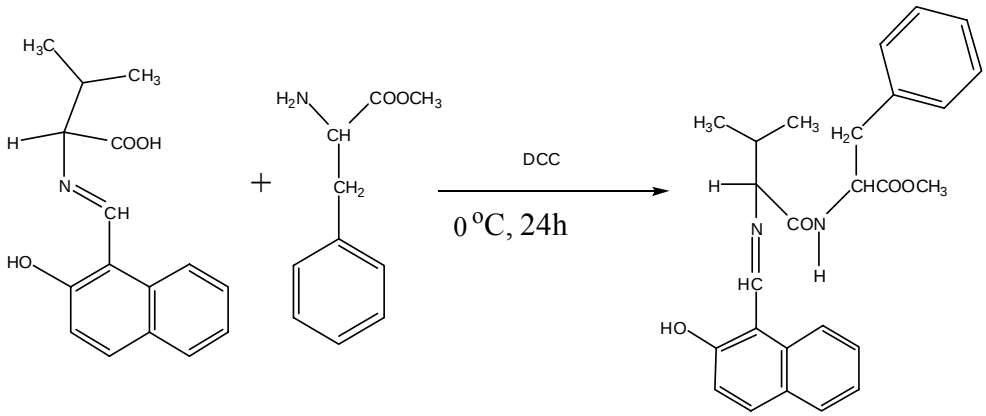


Scheme 5.3 Synthesis of valine - naphthaldehyde Schiff base

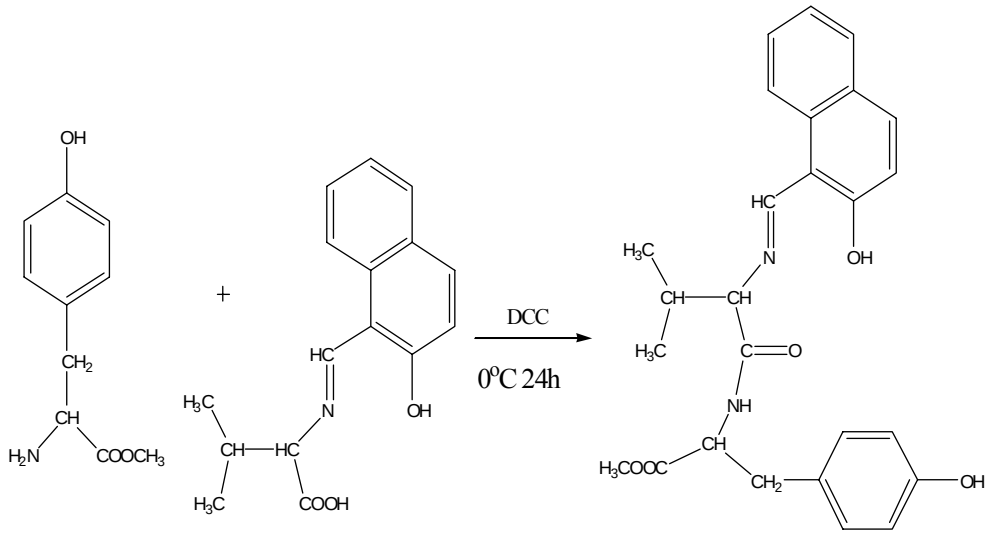
The product was characterized by IR and ^{1}HNMR spectra. The amino acid stereochemistry was maintained after the reaction.

5.2.4 Synthesis of dipeptides

Dipeptides of amino acids were synthesized by reacting equimolar mixture of schiffs base of amino acids and amino acid methyl esters at 0^{o}C for 24h. DCC was used as the coupling agent. Phenylalanine methyl ester and tyrosine methyl ester were used for preparing the dipeptides using valine-naphthaldehyde Schiff base. The crude product was filtered through celite. Pure products were obtained by column chromatography using silica gel column and hexane: dichloromethane as eluent (8:2v/v). Scheme 5.4 & 5.5



Scheme 5.4 Synthesis of valine-naphthaldehyde phenylalanine methyl ester dipeptide (Naph val-phe-OMe) (DP2)

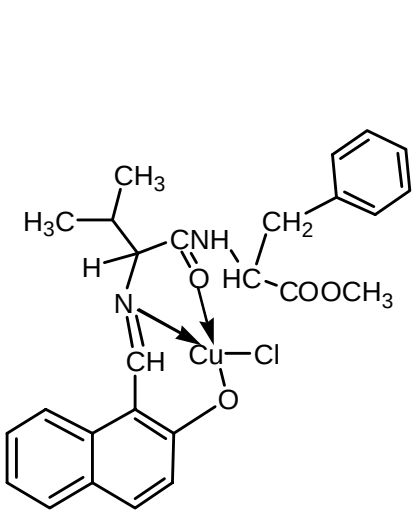


Scheme 5.5 Synthesis of valine-naphthaldehyde tyrosine methyl ester dipeptide (Naph-val- tyr OMe) (DP3)

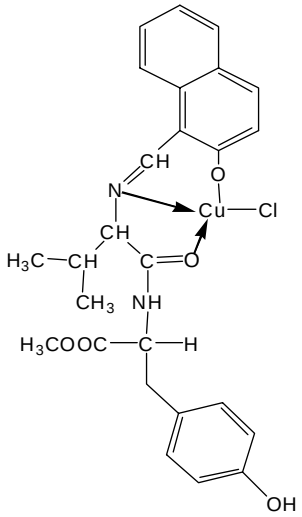
The dipeptides 2 & 3 were charactersied by determining melting points, IR, ^{1}HNMR and mass spectra. Attempts to get sufficiently large crystals suitable for recording X-ray diffraction patterns failed. NMR spectra indicated the absence of racemization.

5.2.5 Preparation of dipeptide metal complexes of Copper and Titanium

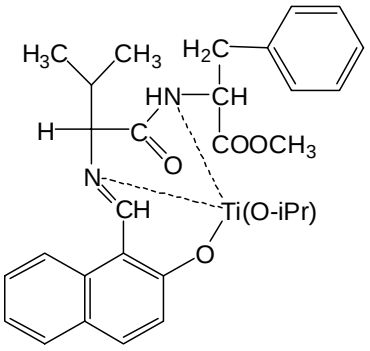
The metal complexes of dipeptides DP_2 and DP_3 were prepared by reacting equimolar mixture of dipeptide and metal salt in dichloromethane under N_2 atm. Yellow colored solid was obtained for complex of titanium and green coloured solid was obtained for copper complexes of dipeptides. The tentative structures of the complexes are shown in fig. 5. 3. The metal complexes were characterized by FT IR spectroscopy.



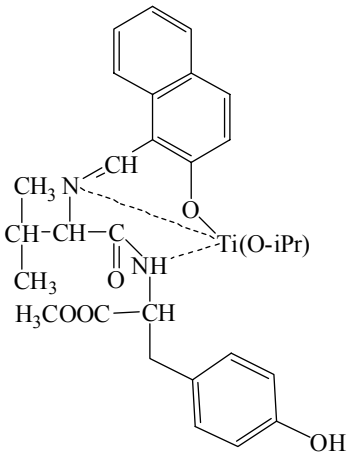
DP2Cu



DP3Cu



DP2TiP



DP3TiP

Fig. 5.3 Tentative structures of dipeptide metal complexes

5.2.6 Characterisation of dipeptide metal complexes

5.2.6.1 FT-IR spectra of complexes

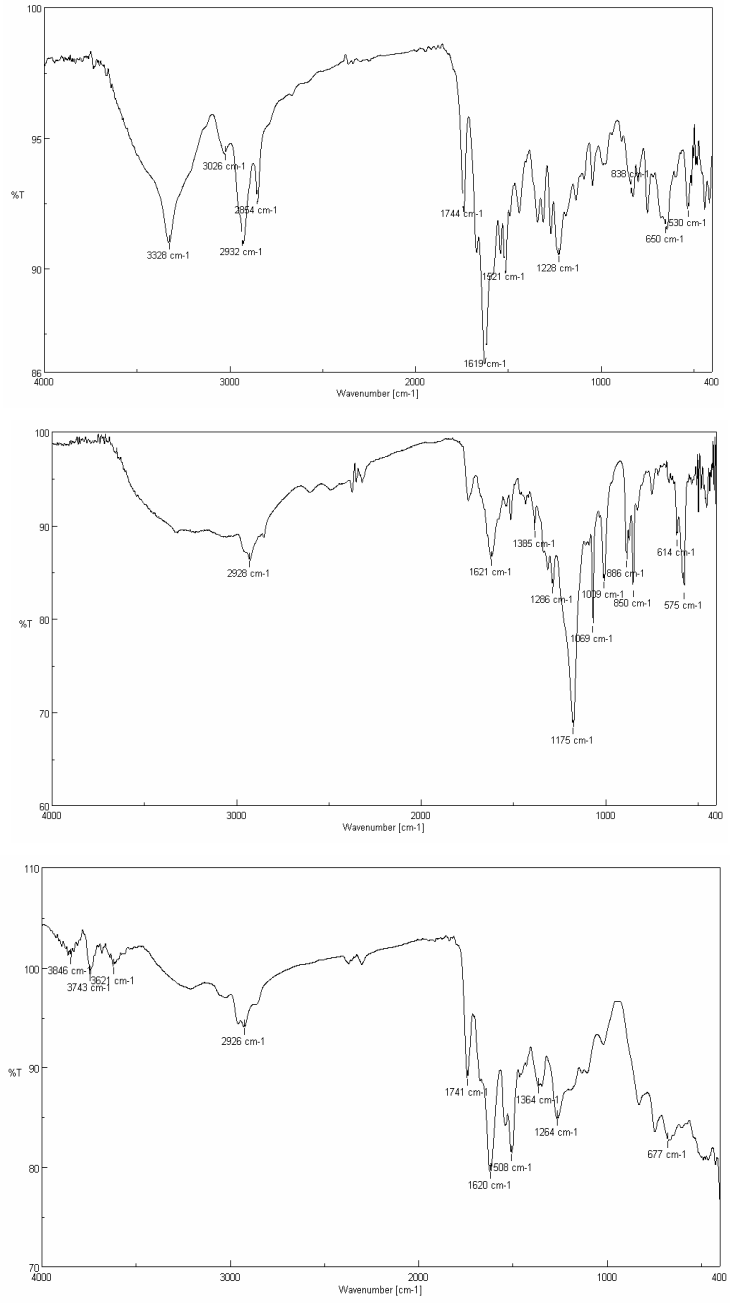


Fig. 5.4 FT-IR Spectra of DP3, DP3Cu and DP3TiP

IR spectra of the complexs and free ligand exhibited a broad band in the region 3300-3400cm^{-1}, which can be attributed to the stretching vibration of the OH group [31]. The C=N imine stretching vibration was observed in the region 1619-1655cm^{-1} for the free ligand, clearly indicating the formation of Schiff bases. When the spectra of the complexes are compared with those of the free Schiff base ligands, the υ(C=N) band observed at 1650cm^{-1} was shifted to a lower frequency (1620cm^{-1}), indicating that the imino nitrogen has coordinated to the metal ion. The negative shift of 30 cm^{-1} for the band indicated weakening of the C-N bond [32].

In the FT-IR spectra of complexes, the asymmetric and symmetric carbonyl stretching vibration bands are shifted to higher frequency indicating the formation of a linkage between a metal ion and the carbonyl oxygen [33]. Other sets of characteristic absorption bands appear in the region 1223 and 1521cm^{-1}. These can be assigned to phenolic C-O and amide N-H stretching vibrations for the free ligand respectively. The phenolic stretching C-O and amide N-H stretching are shifted to a higher frequency upon complexation, implying that the phenolic oxygen and amide nitrogen on the dipeptide form coordinate bond with the metal ions [34-35]. Conclusive evidence regarding the bonding of the nitrogen and oxygen is provided by the occurrence of bands at 587-515cm^{-1}(M-N) and 507-424cm^{-1}(M-O) [36] (fig.5.4).

5.2.6.2 Electronic spectra

The electronic absorption spectra of the metal complexes were recorded in methanol. The divalent metal complex absorption bands of strong intensity corresponding to C=N chromophore occur at 200-300 nm. These bands are attributed to π- π* transitions of the extended conjugation system formed by the benzene ring, phenolic oxygen and imino nitrogen confirming the formation of Schiff base metal complexes [37]. From the Fig.5.5 it can be seen that only complexes of copper shows peak in this region. The band at,

353, 388, 413 nm have been assigned to n- π* transitions of the C=N chromophore, coupled with the secondary band of the benzene ring [38].

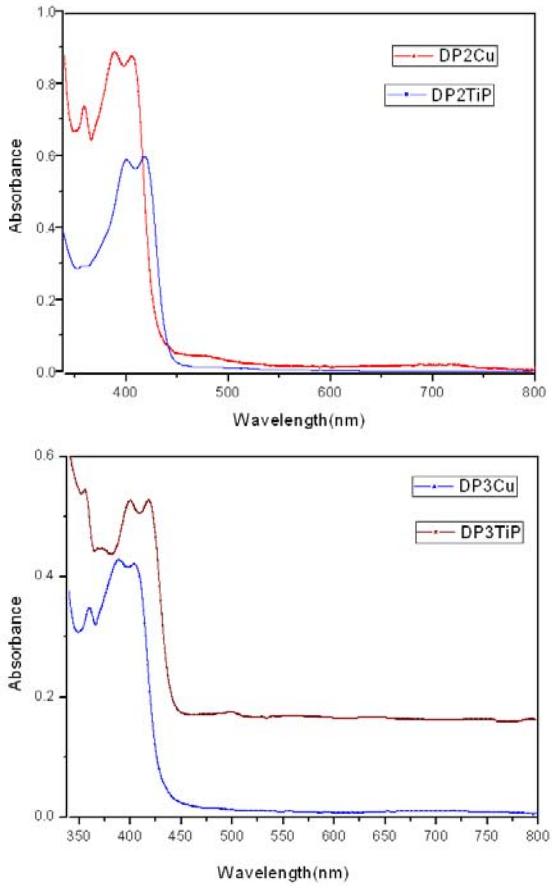


Fig. 5.5 Electronic spectra of dipeptide Schiff base complexes of DP2 and DP3

5.2.7 Preparation of clay supported dipeptide – metal ion complexes

Activated K10 clay swollen in water was stirred with 2M solution of NaNO3 overnight. The sodium exchanged clay so obtained was washed with deionized water repeatedly till the filtrate was free from nitrate ions; the clay was dried in air oven for 2h at 150°C. Sodium exchanged clay was stirred with 20 wt% of the dipeptide metal complexes in CH2Cl2 under N2 atmosphere and dried at 100°C for 2h. Tentative structure of the Cu and Ti complexes supported on clay are given in fig. 5.6

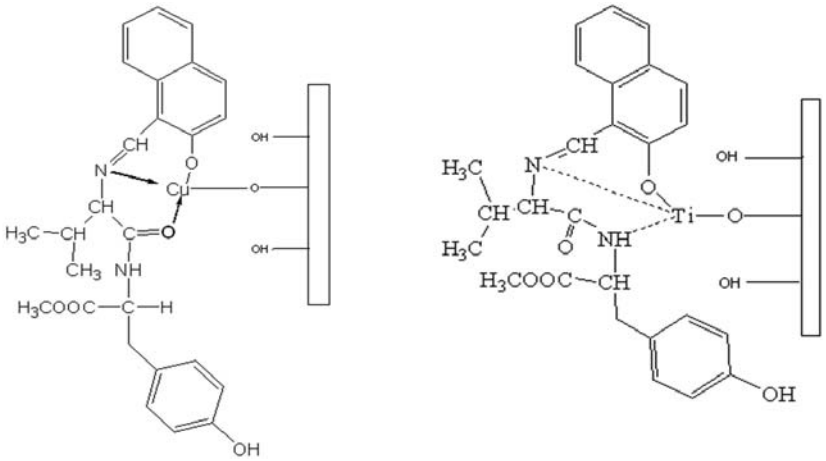


Fig. 5.6 Tentative structure of Cu and Ti complexes supported on clay

5.2.7.1 Characterization of the catalyst

The thermal stability of the selected catalyst was studied using thermogravimetric anlaysis. The catalyst was subjected to thermogravimetric analysis in the temperature range 50-800°C using a linear temperature programme at a heating rate of 10°C/min. Thermogram of the samples shows a weight loss around 230°C which may be due to the loss of organic part. The TG/DTA profiles of K10DP3Cu is shown in (Fig 5.7)

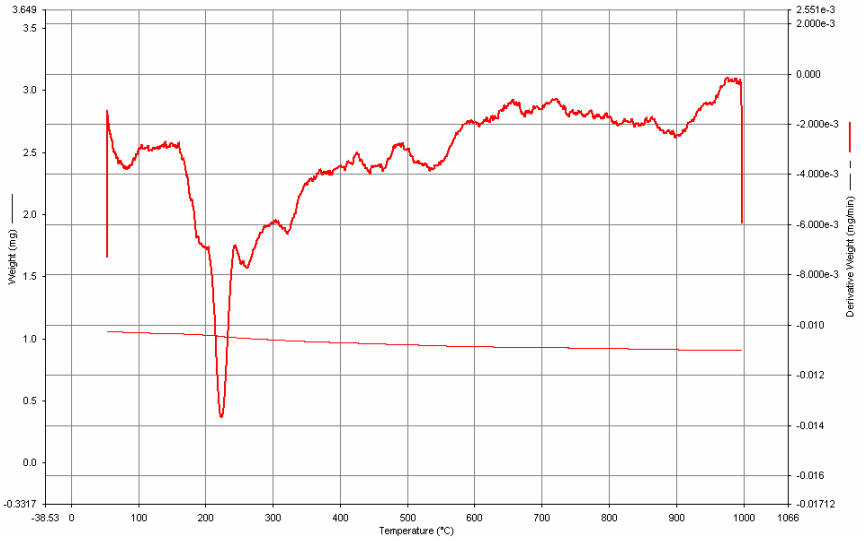


Fig. 5.7 TG/DTA plot of DP3Cu

Table 5.1 EDX data of K10DP3Cu

Element	(keV)	Mass%	Atom%	K
C K	0.27	3.86	6.8	
O K	0.53	39.4	52.07	1.30
Na K	1.041	0.05	0.05	0.97
Mg K	1.2	1.24	1.08	0.94
Al K	1.48	9.35	7.33	0.98
Si K	1.74	40.21	30.28	1
K K	3.31	1.13	0.61	1.48
Fe L	0.70	4.57	1.73	4.80
Cu K	8.04	0.19	0.06	4.87
Total		100	100	

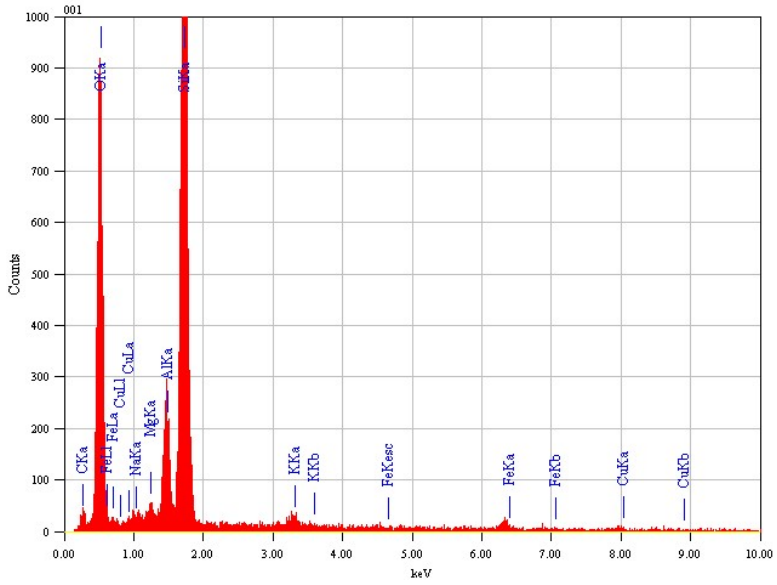


Fig. 5.8 EDX spectra of K10DP3Cu

The metal content of the catalysts was estimated using electron disperse X-ray microscope (EDX) connected to a JOEL microscope. The presence of copper was confirmed in the catalyst. The results are shown in table 5.1and fig 5.8

The amount of copper present in the catalyst was also estimated by ICP-AES. The results are shown in table 5.2. The K10DP3Cu catalyst contains 0.2 % of copper.

Table 5.2 ICP-AES result of K10DP3Cu

	Al	Ca	Cu	Mg	Si	K	Fe	Na
K10DP3Cu	12.1	2.9	0.20	2.7	62.2	4.1	7.2	2.2

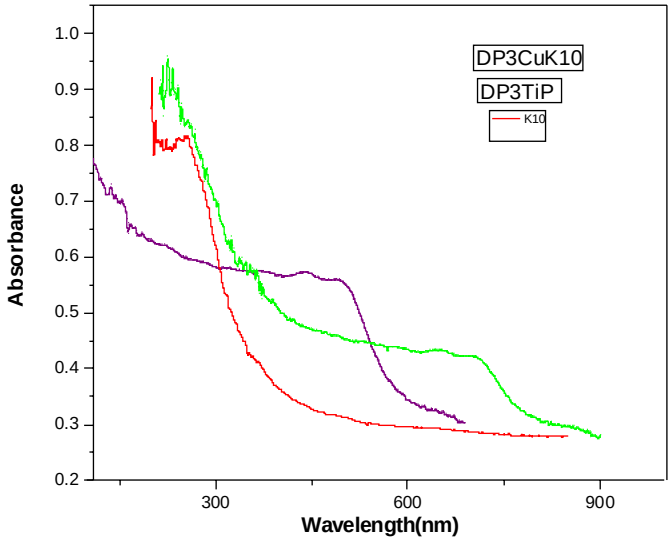


Fig 5.9 UV-DRS spectra of catalysts derived from DP3

The UV-DRS spectra of the parent Montmorillonite K10, supported copper complex and supported titanium complex catalysts are shown in Fig 5.9. UV-DRS Spectra of the catalysts are characterized by broad absorption band centered around 400-500nm in the copper catalysts and 260-270nm and above 300 nm in the case of titanium catalysts. The parent Montmorillonite K10 shows no absorption band in this region (fig 5.9).

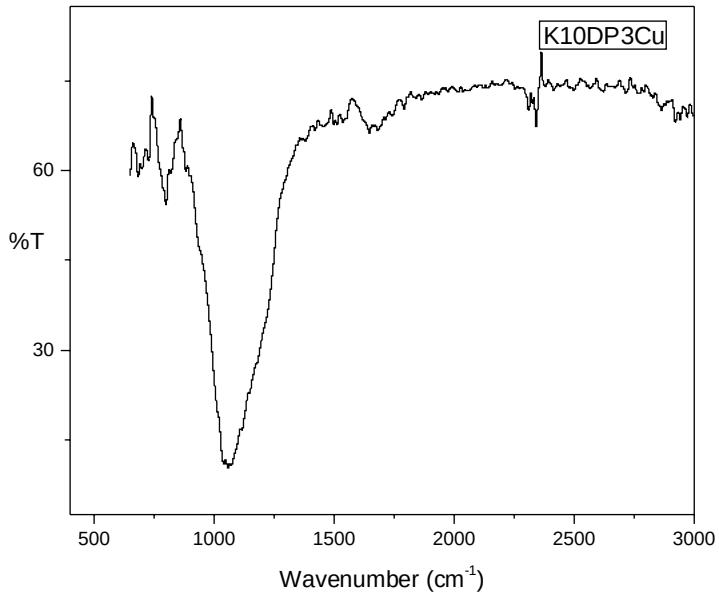


Fig 5.10 FT-IR Spectra of K10DP3Cu

FT-IR spectra of K10DP3Cu catalyst showed a weak broad peak in the region 1600cm^{-1}, characteristic of carbonyl absorption of the dipeptide fig 5.10.

5.2.8 Aza-Diels Alder reaction

5.2.8.1 Screening of the Catalyst in Aza-Diels Alder reaction

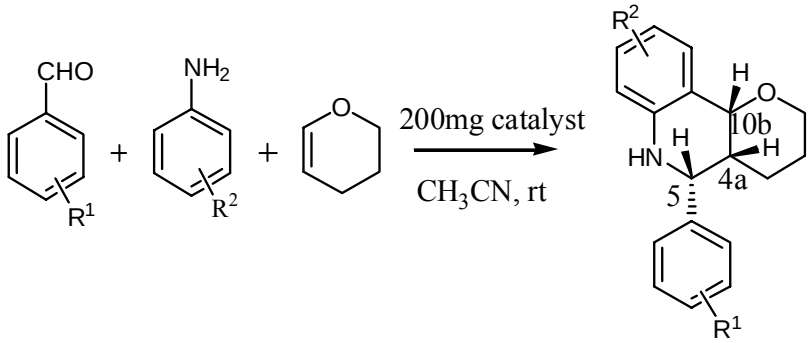
The catalysts were screened for Aza-Diels Alder reaction and the results are summarized in table 5.3, better result was obtained for K10DP3Cu and was selected as the catalyst of choice.

Table 5.3 Screening of the catalyst for Aza-Diels Alder reaction

Catalyst	Metal ion	% Yield
DP2	Cu^{2+}	48
	Ti^{4+}	52
DP3	Cu^{2+}	79
	Ti^{4+}	68

The prepared catalysts were tested by taking benzaldehyde (1mmol), 3, 4-dihdropyran (1mmol), and aniline (1mmol) and 200 mg of the catalyst in the Aza-Diels Alder reaction. The maximum yield was obtained for the catalyst K10DP3Cu.

The Aza-Diels Alder reaction was carried out with K10DP3Cu. Aldehyde (1mmol), amine (1mmol) and 3,4-dihydropyan or 2,3-dihydrofuran (1mmol) were reacted with 200 mg of the catalyst. Imines generated in situ from aldehydes and amines, immedietly reacted with dihydropyran to afford pyrano[3,2-c]quinolines in one pot without the need of preformation of the imines. It was found that the reaction of benzaldehyde, aniline and 3, 4-dihydro-2H-pyran was efficiently catalysed by K10DP3Cu. The reaction did not occur in the absence of catalyst. Regardless of the electronic properties or steric hindrance of the substituents on the aromatic ring of aldehydes, ring-fused [3,2-c] quinolines were obtained in good to excellent yield with high enantioselectivity.



Scheme 5. 6 General scheme of Aza-Diels Alder reaction

Various solvents were used in the model reaction with K10DP3Cu (200 mg) as catalyst; the results are summarized in table 5.4. Acetonitrile was the best solvent among those tested. Several amines and aldehydes were examined, and the results are listed in table 5.5. In all cases, the three component one pot reaction proceeded smoothly to give the corresponding pyrano/ furano [3,2-c] quinolines.

Table 5.4 Effect solvent on Aza-Diels Alder reaction

Sl.No	Solvent	% Yield of the product
1	$CHCl_3$	76
2	C_2H_5OH	78
3	CH_3OH	82
4	CH_3CN	84
5	H_2O	79

Reaction condition: Reactions were carried out with benzaldehyde (1 mmol), aniline (1 mmol),
2, 3-dihydropyran (1 mmol), 200 mg catalyst, at room temperature for 12 h under N_2 atmosphere.

Table 5.5 Aza-Diels Alder reaction with various substrates

Entry	RCHO	RNH_2	Olefin	Yield (%)[a]	M.p ^oC	ee(%)[b]
1	Benzaldehyde	Aniline	3,4-dihydropyran	79	120	83
2	3-Nitrobenzaldehyde	Aniline	3,4-dihydropyran	68	180	99
3	4-Chloro Benzaldehyde	Aniline	3,4-dihydropyran	71	163	82
4	Benzaldehyde	4-Bromo aniline	3,4-dihydropyran	78	147	81
5	Thiophene carboxaldehyde	Aniline	3,4-dihydropyran	76	145	87
6	4-Methoxybenzaldehyde	Aniline	3,4-dihydropyran	81	-	83
7	Benzaldehyde	Aniline	2,3-dihydrofuran	78	108	81
8	3-Nitrobenzaldehyde	4-Bromo aniline	2,3-dihydrofuran	64	184	89
9	4-Chlorobenzaldehyde	Aniline	2,3-dihydrofuran	66	78	81
10	3-Nitrobenzaldehyde	Aniline	2,3-dihydrofuran	62	159	73

Reactions were carried out with 1mmol aldehyde, 1mmol amine, 1mmol olefin, 200 mg catalyst, in acetonitrile at room temperature 12 h under N_2 Atmosphere.

a) Isolated yield of purified product
b) Determined by HPLC with chiral OJ-H column

The products were characterized by determining the m.p and comparing the IR and ^{1}HNMR spectra were used to establish the cis ring fusion. In the ^{1}HNMR spectra, for the signals at ~5ppm, the coupling constant ($J_{4a,\ 5}$) = 5.2 Hz is small and typical for a guache confirmation of the protons, consistent with all cis-configuration of the hydrogen atoms 4a, 5 and 10b. The coupling constant ($J_{4a,\ 10b}$) in all products (2.2-2.9 Hz) indicates the cis fusion of the pyran-and quinoline rings.

5.2.8.2 Recycling studies

After completion of the reaction the catalyst was filtered, washed with acetone, methanol and ethyl acetate repeatedly followed by drying at 100^{o}C for 1h and reused. The catalyst activity was found to be decreased upon each cycle. The results of recycling studies are summarized in table 5.6

Table 5.6 Recycling studies of the catalyst

Entry	No. of recycling steps	% Yield[a]
1	1	61
2	2	46
3	3	37

Reaction condition: Benzaldehyde (1 mmol), aniline (1 mmol), 3, 4-dihydropyran (1 mmol), Catalyst 200 mg, Solvent: acetonitrile (5ml) Time: 12h [a]Isolated yield

5.2.8.3 Conclusion

K10 clay supported dipeptide schiffs base complexes of copper and Ti were synthesized conveniently from natural amino acids and their catalytic activity were investigated in Asymmetric Aza Diels alder reaction. The amount of catalyst required was low, good yields and high enantioselectivity were obtained in all the cases studied.

5.3 Experimental

5.3.1 Preparation of amino acid esters

Thionyl chloride (0.5ml) was added to methanol (20ml) in a 50ml RB flask fitted with a reflux condenser and cooled in an ice-salt water bath to about -10°C (internal temperature). Amino acid (5 mmol) was added. Ice bath was removed and the mixture was heated to reflux for 2h. The mixture was concentrated in a rotary flash evaporator to about 2-5ml. The product was precipitated by the slow addition of peroxide free ether. Pure product was recrystallised from methanol/ether.

5.3.2 Preparation of Naphthaldehyde Schiff bases of amino acids

To a suspension of valine (20 mmol) in a mixture of ethanol (500 ml) and methanol (40 ml) was added 2-hydroxynaphthaldehyde (30 mmol). After being stirred for 16h, the resulting yellow solution was concentrated under vacuum to leave the mixture of N-2- hydroxy-1-naphthaldehyde. The residue was washed well with ether to remove the excess 2-hydroxy-1-naphthaldehyde. The product was obtained by filtration to yield yellow solid Schiff base of of 2-hydroxy-1-naphthaldehyde of amino acids.

5.3.3 Preparation of dipeptides

5.3.3.1 N-(2hydroxy-1-napthyl)methylene)-(L)-valyl-(S)-phenylalanine methyl ester(Nap-L-Val-L-Phe-OMe)[DP-2]

To a suspension of (L)-valine (2.34g, 20 mmol) in a mixture of ethanol (500ml) and methanol (40ml) was added 2-hydroxy-1-naphthaldehyde (5.17 g, 30 mmol). After being stirred for 16h, valine had dissolved, and the resulting yellow solution was concentrated in vacuo to leave the mixture of N-((2-hydroxy-1-naphthyl)methylene)-(L)-valine and excess of 2-hydroxy-1-naphthaldehyde. The residue was washed well with ether to remove the excess 2-hydroxy-1-naphthaldehyde by filtration to yield a yellow solid of N-((2-hydroxy-1-naphthyl) methylene)-(L)-valine (5g, yield 92.2 %). To a solution

of L-phenyl alanine methyl ester hydrochloride (1.24g, 6mmol) in water (10 ml) was added potassium carbonate (1.24 g, 9mmol). After the mixture was stirred at room temperature for 10 min, the aqueous layer was extracted with ether (20mlx5). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo to afford free (L)-phenylalanine methyl ester as viscous oil (0.9 g. 5mmol). To a suspension of N-((2-hydroxy-1-naphthyl) methylene)-(L)-valine(1.5g, 5mmol), in dichloromethane(30mL) was added N,N'dicyclohexylcarbodiimide (DCC) (1.03g, 5mmol) at 0°C followed by freshly prepared (L)-phenylalanine methyl ester (0.9g, 5mmol). The reaction mixture was stirred at 0°C of 1h and at room temperature for 24h; the resulting white precipitate of DCU was removed by filtration through celite, and the filtrate was concentrated to give the crude product as a yellow solid which was purified by column chromatography on silica gel (dichloromethane: ethyl acetate, 4:1) to yield.1.16g (48.5%) which was recrystallised from ethanol, mp 243°C.

IR (KBr): 3460, 3200, 3026, 2976, 1740, 1660, 1625, 1540, 1510, 1490, 1430, 1310, 1270, 1140, 1010, 860, 836, 740cm-1

^{1}HNMR ($CDCl_3$): 14.38 (br s, 1H), 9.05 (s, 1H), 8.02 (d, 1H, J=8.1Hz), 7.6(d, 1H, J=9.4 Hz), 7.7(d, 1H, J=7.3Hz), 7.4-7.5(m, 1H), 7.32-7.38(m, 1H), 7.13-7.28(m, 6H), 6.42(d, 1H, J=7.6Hz), 4.8-4.9(m, 1H), 3.73(d, 1H, J=4.3Hz), 3.68(s, 3H), 3.3(qd, 1H, J=13.6, J=5.6Hz), 3.0 (qd, 1H, J=13.7, J= 7.7Hz), 2.39-2.51(m, 1H), 0.88(d, 3H, J=6.68), 0.82(d, 3H, J=6.8Hz)

5.3.3.2 N-(2-hydroxy-1-napthyl)methylene)-(L)valyl-(L)-tyrosine methyl ester(Nap-L-Val-L-Tyro-OMe)[DP3]

To a solution of L-tyrosine methyl ester in dichloromethane (1.2g, 6mmol) in water (10mL) a suspension of N-((2-hydroxy-1-naphthyl) methylene)-(L)-valine (1.5g, 5mmol), in dichloromethane (30 mL) was added N,N'dicyclohexylcarbodiimide (DCC) (1.03g, 5mmol) at 0°C followed by freshly prepared (L)-tyrosine methyl ester (0.9g, 5mmol). The reaction mixture was stirred at 0°C of 1h and at room temperature for 24h; the resulting white precipitate of DCU was removed by filtration through celite, and the filtrate was

concentrated to give the crude product as a yellow solid which was purified by column chromatography on silica gel (dichloromethane-ethyl acetate, 4:1) to yield.1.38g (55.6%) which was recrystallised from ethanol mp 225-228^{o}C.

IR (KBr):3460, 2945, 2858, 1637, 1499, 1463, 1380, 1265, 1220, 1105, 860, 710, 680cm^{-1}

^{1}HNMR ($CDCl_3$): 14.1 (br s, 1H), 9.0 (s, 1H), 7.86 (d, 1H, J=8.0Hz), 7.6(d, 1H, J= 9.2 Hz), 7.72 (d, 1H, J=7.2Hz), 7.5(m, 1H), 7.32-7.38 (m, 4H), 7.1-7.2 (d, 1H, J=7.2 Hz), 6.8 (d, 1H, J=7.2Hz), 5.1(m, 1H), 5.3(m,1H), 4.81(m, 1H), 4.06(d, 1H, J=), 3.6(s, 3H), 3.29-3.08 (m, 2H), 2.1(m,1H), 1.01(s, 6H)

5.3.4.1 DP_2Cu Complex

The dipeptide DP2 (0.87g, 2mmol) was dissolved in dry dichloromethane (20ml). To this $CuCl_2$ (0.34g, 2mmol) was added. The mixture was stirred for 2h under N_2 atmosphere. After reaction, the product was filtered and washed with methanol (20ml x 2 times) and dry ether (20ml x 2 times). Drying under vacuum afforded the DP_2Cu (0.6g, 56%).

5.3.4.2 DP_2TiP complex

The dipeptide DP2 (0.87g, 2mmol) was dissolved in dry dichloromethane (20ml). To this Ti (O-i-Pr)$_4$ (0.5 ml, 2mmol) was added. The mixture was stirred for 2h under N_2 atmosphere. After reaction, the product was filtered and washed with methanol (20ml x 2times) and dry ether (20ml x 2times). Drying under vacuum afforded the DP_2TiP (0.7g, 62%).

5.3.4.3 DP_3 Cu complex

The dipeptide DP_3 (0.87g, 2mmol) was dissolved in dry dichloromethane (20ml). To this $CuCl_2$ (0.34g, 2mmol) was added. The mixture was stirred for 2h under N_2 atmosphere. After reaction, the product was filtered and washed with methanol (20ml x 2times) and dry ether (20ml x 2times). Drying under vacuum afforded the DP_3Cu(0.72 g, 67%).

5.3.4.4 DP_3TiP complex

The dipeptide DP_2 (0.87g, 2mmol) was dissolved in dry dichloromethane (20ml). To this $CuCl_2$ (0.5ml, 2mmol) $CuCl_2$ was added. The mixture was stirred for 2h under N_2 atmosphere. After reaction, the product was filtered and washed with methanol (20ml X 2times) and dry ether (20ml X 2times). Drying under vacuum afforded the DP_3TiP (0.87g, 74%).

5.3.5 Preparation of clay supported dipeptide complex catalysts

The clay supported dipeptide metal complex was prepared by exchange of ions in the inter layer of the clay. The sodium ion exchanged K10 was used for this purpose. 3g of activated montmorillonite K10 clay was swelled in water and stirred with 2M solution of $NaNO_3$ overnight. The sodium exchanged clay so obtained after purification was made to react with 20wt% of the complex in dichloromethane under N_2 atmosphere. The catalyst so obtained was used of Aza-Diels Alder reaction.

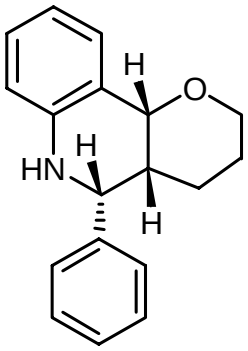
5.3.6 General procedure for Aza-Diels Alder reaction

To a suspension of aldehydes (1mmol), amine (1mmol) in acetonitrile (5 ml), at room temperature, 200 mg of the catalyst (K10DP3Cu) was added. The mixture was stirred for 10 min at room temperature. 3,4-dihyro-2H-pyran or 2,3-dihydrofuran(1mmol) was added. The mixture was further stirred for 12 h. After the reaction it was filtered through a short plug of silica gel. After evaporation of the filtrate, the residue was chromatographed using hexane: ethyl acetate (9:1) on silica gel column to afford the pure products.

In the reaction of benzaldehyde, aniline and 3, 4-dihydro-2H-pyran the elution using hexane: ethyl acetate (9:1 v/v) afforded the major product (1) with an yield of 84%. A minor product (12%) was also isolated. It is marked as 2. The difference between 1 and 2 is the difference in stereochemistry at 5 in 1, it is R and for 2 it is S.

Characterisation of products

Entry 1 table 5.5

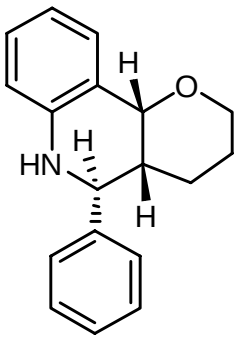


..... (1)

(4a*R*,5*R*,10b*R*)-3,4,4a,5,6,10b-hexahydro-5-phenyl-2*H*-pyrano[3,2-*c*]quinoline

^{1}HNMR (400 MHz; $CDCl_3$): δ 1.25–1.50 (m, 4H), 2.15 (m, 1H), 3.58-3.85 (m, 3H), 4.68 (d, 1H, J=2.6Hz), 5.31(d, 1H, J=5.6Hz), 6.68 (dd, 1H, J=7.8, 0.9 Hz) 7.03 (tt, 1H, J= 7. 6, 0.6Hz), 7.43-7.25(m, 6H).

Entry 1 Table 5.5

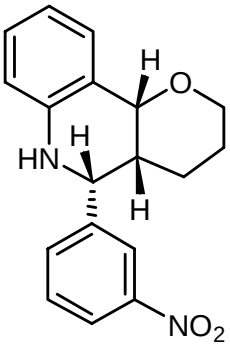


..... (2)

(4a*R*,5*S*,10b*R*)-3,4,4a,5,6,10b-hexahydro-5-phenyl-2*H*-pyrano[3,2-*c*]quinoline

^{1}HNMR (400 MHz; $CDCl_3$) δ 1.250 (m, 1H), 1.48 (m, 2H), 1.66(m, 1H), 1.83(m, 1H), 2.11(m, 1H), 3.71(td, 1H, J=11.6, J=2.5Hz), 4.08(m, 2H), 4.39(d, 1H, J= 2.7Hz), 4.72(d, 1H, J=10.8Hz), 6.51(dd, 1H, J=7.1, 1Hz), 6.7(td, 1H, J=7.0, 1.1Hz), 7.25(dd,1H, J=7.1, 0.5Hz), 7.42-7.36(m,5H)

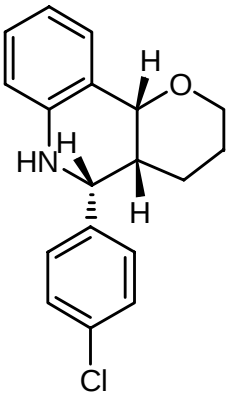
Entry 2 Table 5.5



(4aR,5R,10bR)-3,4,4a,5,6,10b-hexahydro-5-(3-nitrophenyl)-2H-pyrano[3,2-c]quinoline

^{1}HNMR (400 MHz; $CDCl_3$): □̃ı₁□m, 2H), 2.2(s, 1H), 3.58-3.62(m, 5H), 3.9(s,1H), 4.8(d, 1H, J=2Hz), 5.3(d, 1H, J=5.6Hz), 6.65(d, 1H, J=6.7Hz), 6.83(td, 1H, J=7.2Hz), 7.11(tt, 1H, J=7.6Hz), 7.43-7.58(m, 5H), 7.7(d, 1H, J=7.6Hz), 8.16-8.19(dd, 1H, J=9.6Hz, J=1.6Hz), 8.33(s, 1H).

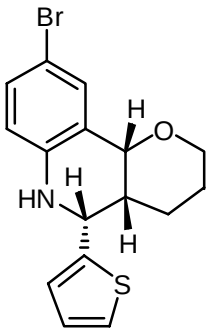
Entry 3 table 5.5



(4aR,5R,10bR)-5-(4-chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline

^{1}HNMR (400 MHz; $CDCl_3$): δ 1.25–1.55 (m, 4H), 2.13–2.15 (m, 1H), 3.42-3.60(m, 2H), 3.80 (s, 1H) 4.6 (d, 1H, J= 5.6Hz) 5.30–5.32 (d, 1H, J=5.6Hz) 6.59(dd, 1H, J= 1.2, 0.8Hz), 6.78-6.82 (td, 1H, *J* = 7.6, J=0.8 Hz), 7.07- 7.1 (dt, 1H, J= 2, 1.2 Hz), 7.44 (d, 1H, *J* = 8 Hz),

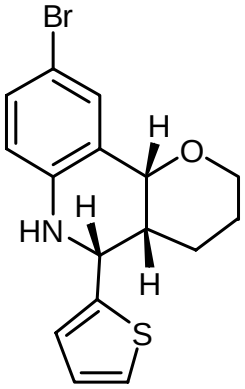
Entry 4 table 5.5



(4aR,5R,10bR)-9-bromo-3,4,4a,5,6,10b-hexahydro-5-phenyl-2H-pyrano[3,2-c]quinoline

^{1}HNMR (400 MHz; $CDCl_3$): δ 1.31–1.52 (m, 4H), 2.14–2.16 (m, 1H), 3.41-3.44(m, 1H), 3.5-3.6 (m, 1H), 3.8(s, 1H), 4.65 (d, 1H, J= 2.8 Hz) 5.26–5.28 (d, 1H, J=5.2Hz) 6.4-6.6(d, 1H, J= 8.4Hz), 7.15-7.17 (dd, 1H, *J* = 8, J=4 Hz), 7.31- 7.38 (m, 5H), 7.52 (d, 1H, *J* = 2 Hz),

Entry 5 Table 5.5



^{1}HNMR (400 MHz; $CDCl_3$): δ 1.48–1.61 (m, 5H), 2.2 (m, 1H), 3.40 (m, 1H), 3.6(m, 1H), 4 (s, 1H) 4.97 (d, 1H, J= 4 Hz) 5.9 (d, 1H, J= 4Hz) 6.59 (d, 1H, J= 8 Hz), 6.8 (td, 1H, *J* = 8, J= 4 Hz), 7.06 (t, 1H), 7.09-7.11(m, 3H), 7.23-7.25 (dd, 1H, *J* = 8Hz, *J* = 4 Hz), 7.42 (d, 1H, *J* = 7.4 Hz),

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Chapter 6

CONVENTIONAL AND MICROWAVE ASSISTED SYNTHESIS OF FEW HETEROCYCLES

Contents

The expeditious and solvent free approach involves the exposure of neat reactants to microwave (MW) irradiation in conjunction with the use of supported reagents or catalysts which are primarily of mineral origin. The solvent free conventional and microwave assisted synthesis of few pharmaceutically important heterocycles and a comparison of conventional and microwave assisted method is explained in this chapter.

6.1 Introduction

Non classical heating technique using microwaves, termed "Bunsen burner of the 21st century", is rapidly becoming popular and is dramatically reducing reaction times. The use of emerging microwave-assisted techniques in conjunction with greener reaction media is dramatically reducing chemical waste and reaction times in several organic syntheses and chemical transformations. The possibility of performing reactions in a short time by

direct interaction of microwave energy with the reaction mixture as opposed to the indirect transfer of energy by utilizing an oil bath or similar device certainly can be considered "green", not only because of the reduced energy consumption, but also because of the associated time savings, thereby increasing efficiency. There is a variety of approaches for the development of sustainable methods, which reflect the enormity and complexity of this field. Twelve Principles of Green Chemistry [1] has been given by Paul Anastas and John Warner in 1998. Fifth principal states that, "the use of auxiliary substances (solvent etc) should be made unnecessary wherever possible and, innocuous when used". Sixth principal states that, "energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure". Among the 12 principles of green chemistry, the desire for utilizing "safer solvents" and to "design for energy efficiency" can be considered two important key principles of relevance to synthetic chemists.

6.2 Microwave Chemistry

Microwaves lie in the electromagnetic spectrum between infrared waves and radio waves. They have wavelengths between 0.01 and 1 meter, and operate in a frequency range between 0.3 and 30 GHz. However, for their use in laboratory reactions, a frequency of 2.45 GHz is preferred, since this frequency has the right penetration depth for laboratory reaction conditions. All domestic microwave ovens, microwave reactors and other laboratory and industrial systems usually work at 2.45 GHz.

6.2.1 Interaction of microwave radiation with materials

The mechanism of energy transfer in a microwave is significantly different from a hotplate or heating mantle. Microwave energy heats the sample through direct activation. In the microwave, energy is transferred to the reaction components within the solution. There are two components of a

microwave: an electric field and a magnetic field. The electric field will interact with any molecule that has a dipole or that is ionic. The electric field component causes heating by two main mechanisms viz.,(i) Dipolar polarization (Fig. 6.1) and (ii) Ionic conduction (Fig 6.2) The interaction of electric field component with polar molecules is called the dipolar polarization mechanism.

Fig. 6.1 Dipolar interaction

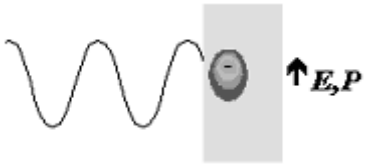


Fig. 6.2 Ionic conduction

When exposed to microwave frequencies, the molecular dipoles align in the applied electric field. As the applied field oscillates, the dipole field attempts to follow these oscillations and the energy is lost in the form of heat through molecular friction and dielectric loss. The amount of heat generated by this process is directly related to the ability of the molecules to align itself with the frequency of the applied field [2]. The second major heating mechanism is the ionic conduction. During ionic conduction, the dissolved charged particles in a sample (usually ions) oscillate back and forth under the influence of the electric component of microwave irradiation. They collide with their neighboring molecules or atoms. These collisions cause agitation or motion, creating heat. Most pioneering experiments in chemical synthesis using microwaves were carried out in domestic microwave ovens. However, developments in microwave equipment technology have enabled researchers to use dedicated apparatus for organic reactions.

6.3 Microwave assisted organic synthesis

Use of Microwave Ovens for Rapid Organic Synthesis was demonstrated for the first time in 1986 by Gedye et al. [3]. They studied the

utilization and advantages of microwave irradiation for organic synthesis involving hydrolysis of benzamide to benzoic acid under acidic conditions. Rate of reaction increased considerably (5 - 1000 fold) for the transformations compared to classical thermal reflux conditions.

The advantages of using microwave dielectric heating for performing organic reactions were realized thereafter by many different groups and as a consequence the amount of articles describing high-speed chemical synthesis promoted by microwave irradiation has grown quickly from ~200 in 1995 to ~1000 in 2001[4]. There are a number of reviews available in the literature on the subject: Microwave-Assisted synthesis in water as solvent by Dallinger et al [5], controlled microwave heating in modern organic synthesis by Kappe et al.[6], aqueous microwave chemistry: a clean and green synthetic tool for rapid drug discovery by Polshettiwar et al.[7] and microwaves in organic synthesis - thermal and non-thermal microwave effects by Hoz et al[8]. A number of Solvent-free organic synthesis using supported reagents and microwave irradiation has been reported [9-11]. In the present work, synthesis of 2,4,6-triaryl pyridines and imidazoles under solvent free synthesis using conventional and microwave heating methods are studied in detail.

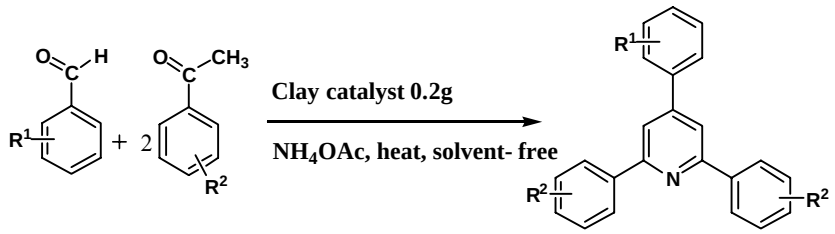
6.4 Triarylpyridine synthesis using conventional heating under solvent free conditions

One-pot multicomponent coupling reactions (MCRs),where several organic moieties are coupled in one step, for carbon-carbon and carbon–heteroatom bond formation is an attractive synthetic strategy for the synthesis of small–molecule libraries with several degrees of structural diversities[12]. Multi aryl substituted pyridine derivatives are recently reported as electron transport materials [13]. The highly substituted pyridine derivatives, like 2-amino-4-aryl-3, 5-dicyano-6-sulfanylpyridines have significant and diverse medicinal utility. Essentially, these compounds serve as high-potency agonists

for the human adenosine receptors and act as potential therapeutic agents for the treatment of Creutzfeldt–Jacob disease, Parkinson's disease, hypoxia, asthma, cancer, kidney disease and prion disease [14-16]. Due to their π-stacking ability, some pyridines are used in supramolecular chemistry [17-19]. Previously, 2,4,6-triarylpyridines have been prepared by the condensation of 1,5-diketones with formamide –formic acid [20], reaction of (aroylmethylene) isoquinolinium ylide with α,β-unsaturated ketones [21-22], and reaction of N-phenacylpyridinium salts with α,β-unsaturated ketones in the presence of ammonium acetate [23]. More recently, many improved methods for preparation of 2,4,6-triarylpyridines have been reported such as reaction of α-ketoketene dithioacetals with methyl ketones in the presence of ammonium acetate [24], reaction of N-phosphinylethanimines with aldehydes [25], addition of lithiated β-enaminophosphonates to chalcones [26], condensation of acetophenone, benzaldehyde and NH_4OAc in the presence of NaOH under solvent free condition [27], one pot reaction of acetophenones, benzldehydes and NH_4OAc without catalyst under microwave irradiation [28] etc.

Due to the non corrosive, easy to handle, thermally robust, inexpensive and environmental friendly nature, clays have gained importance in organic synthesis as solid acid catalysts. Montmorillonite K10 has proved to be an efficient catalyst in promoting various organic reactions such as addition reaction [29], Knovenagel condensation [30], Aza-Diels Alder reaction [31], Esterification [32], isomerisation reaction [33] etc. However, the utility of this catalyst for the synthesis of trisubstituted pyridines under solvent free condition has not been explored before. To exploit the catalytic activity of clays for various organic transformations, a one-pot solvent free synthesis of 2, 4, 6-trisubstituted pyridines by condensation of various aldehydes, ketones and ammonium acetate have been attempted under conventional and microwave heating.

The catalytic efficiency of K10 was evaluated for the synthesis of triaryl pyridines by a one pot condensation of aldehyde, ketone and NH_4OAc under solvent free condition. High yield (97%) was obtained with benzaldehyde and acetophenone. To evaluate the scope and limitations of the methodology, reactions were carried out with various substituted benzaldehydes including both electron-donating and electron-withdrawing substituents at para position of the aromatic ring (Table 6. 1). The results showed that there was no adverse effect of substituents, either electron-donating or electron-withdrawing, on the aromatic ring of benzaldehyde or acetophenone on the product yield. In the case of all the aldehydes, high yields (>88%) were obtained in comparatively less time (2–6 h). All the products were characterized by comparing melting points with those of the reported compounds. The reaction conditions such as temperature, time and amount of catalyst were optimized. The effect of catalyst loading was studied by increasing the catalyst concentration from 0.05 g to 0.2 g with an increment of 0.05 g selecting benzaldehyde and acetophenone as substrates for 3h, the formation of product was found to increase up to 0.2 g, further increase did not appreciably affect the yield of the product. Optimum catalyst concentration of 0.2 g was selected for further studies. Similarly temperature was also optimized by varying the temperature from 40-130^oC, optimum temperature obtained was 120^oC.



Scheme 1 Synthesis of 2,4,6-triarylpyridines under solvent free condition (conventional heating)

Table 6.1 Synthesis of 2,4,6-triarylpyridines under solvent free condition (conventional heating)

Entry	R_1	R_2	Time (h)	Yield (%)	M.p (^oC) (lit.)
1	H	H	4	97	133-136(135)[34]
2	H	4-CH_3	6	93	156-158(157-158)[36]
3	H	4-Br	5	92	194-196(192-194)[26]
4	4-OH	H	5	97	197-198(197-198)[34]
5	4-NO_2	H	6	91	203-205(202-203)[34]
6	2-Cl	H	4.5	93	113-114(109-111)[37]
7	4-Cl	H	4	94	126-127(129-130)[34]
8	4-OCH_3	H	7	96	101-102(98)[36]
9	4-CH_3	H	6.5	95	116-118 (116)[35]
10	4-CH_3	4-CH_3	5	90	177-178(178-180)[26]
11	3-NO_2	4-Br	5	89	>200
12	4-Cl	4-CH_3	4	96	199-201(200-202)[36]
13	4-Cl	4-Br	5	94	>200
14	Thiophene	H	4	91	168-170(68-170)[36]
15	Thiophene	4-CH_3	3.5	88	162-163(164-165)[36]

[a]Reaction conditions: Temperature 120^{o}C,Catalyst 0.2 g, aldehyde:NH_4OAc, ketone :1:1.3:2 mmol.
[b]Isolated yield of product.

The effect of various ammonia sources was studied. Effect of the different ammonia derivatives on yield of the product were checked, maximum, yield was obtained for NH_4OAc. Results are summarized in table 6.2

Table 6.2 Effect of various ammonia sources on the yield of product.

Ammonia source	Time(h)	Yield%[b]
NH_4OAc	4	97
NH_2CONH_2	6	40
NH_2COCH_3	5	65
NH_2CSNH_2	4.5	36

[a]Reaction conditions: Temperature 120^{o}C, Catalyst 0.2 g, benzaldehyde:NH_4OAc: acetophenone :1:1.3:2 mmol.
[b]Isolated yield of product.

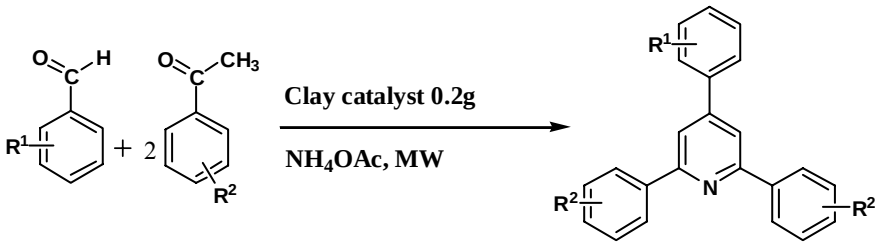
The main advantages of the present method in the synthesis of triarylpyridines are that they are clean reactions without any side product under solvent free condition and work up does not require column chromatography. The catalyst could be recycled efficiently for three cycles without any appreciable loss in the yield

6.4.1 Microwave assisted synthesis of triarylpyridines

The practical feasibility of microwave assisted solvent-free protocols has been demonstrated in useful transformations involving protection/deprotection, condensation, oxidation, reduction, rearrangement reactions in the synthesis of various heterocyclic systems on inorganic solid supports. The absence of solvent reduces the risk of hazardous explosion when the reaction takes place in a closed vessel in an oven; aprotic dipolar solvents with high boiling points are expensive and are difficult to remove from reaction mixtures. During microwave induction of reactions under dry conditions, the reactants adsorbed on the surface of alumina, silica gel, zeolites, clays or similar materials absorb the microwave whereas the support does not, nor does it restrict their transmission. Such supported reagents efficiently induce reactions under safe and simple conditions with domestic microwave ovens instead of commercial microwave systems that require sealed Teflon bombs. The synthesis of triaryl pyridines with montmorillonite K10 has been attempted under solvent free condition using a domestic microwave oven. The effect of microwaves on chemical reactions is evaluated by comparing the time needed to obtain a given yield of the final product in comparison to the conventional heating.

Montmorillonite K10 clay was used for the solventless synthesis of triaryl pyridines. The efficiency of the catalyst in both conventional and microwave heating can be compared. The conventional heating involved heating the reaction mixture with the refluxing vessel in an oil bath. The

microwave heating is employed using the house hold microwave oven (LG model 360 W). The reaction is shown in the scheme 2.



Scheme 2 Synthesis of 2,4,6-triarylpyridine under microwave irradiation.

The preparation of triarylpyridine using microwave irradiation was carried out for different substrates. In all the cases, less time was required for the completion of the reaction under microwave heating and the yield was comparable. The results are summarized in table 6.3

Table 6.3 Synthesis of 2,4,6-triarylpyridine under microwave irradiation

Entry	R_1	R_2	Time (Min)	Yield (%)
1	H	H	5	95
2	H	4-CH_3	4	91
3	H	4-Br	5	93
4	4-OH	H	5	89
5	4-NO_2	H	4	90
6	2-Cl	H	6	87
7	4-Cl	H	4	84
8	4-OCH_3	H	4	84
9	4-CH_3	H	3	85
10	4-CH_3	4-CH_3	5	88
11	3-NO_2	4-Br	5	76
12	4-Cl	4-CH_3	3	84
13	4-Cl	4-Br	3	89
14	Thiophene	H	5	85
15	Thiophene	4-CH_3	5	90

Reaction condition; Aldehede (1mmol), Ketone(2 mmol), ammonium acetate (1.3 mol%), Catalyst=0.2 g, MW, 360W, 3-6 min.

6.4.1.1 Recycling studies of the catalyst

Recycling studies of the catalyst was carried out by taking benzaldehyde (1mmol), acetophenone (2 mmol), ammonium acetate (1.3 mol %), catalyst 0.2 g. The mixture was ground well in a mortar and irradiated at 160W for one minute and at 360W for 6 min. The resulting product was extracted with hot ethanol and recrystallised. The results obtained are shown in table 6.4. It is observed that there is negligible decrease in yield upto three cycles.

Table 6.4 Synthesis of 2,4,6-triarylpyridine under microwave irradiation

Catalyst	Product	Yield of the product %		
K10	Triphenyl pyridine	First cycle	Second cycle	Third cycle
		92	86	80

Reaction condition: benzaldehyde (1mmol), acetophenone (2mmol), catalyst 200mg K10Ti, MW= 360W, 6min.

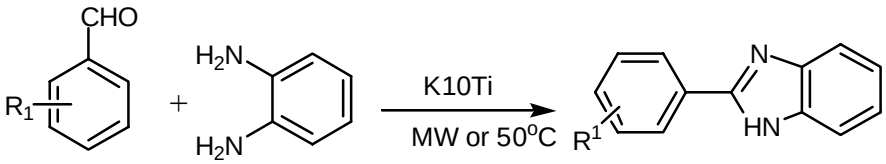
6.4.2 Microwave assisted synthesis of benzimidazoles using K10Ti catalyst

Benzimidazoles are very useful intermediates for the development of molecules of pharmaceutical and biological interest. Substituted benzimidazole derivatives have found applications in diverse therapeutic areas including antiulcers and antihistaminics [38-40]. Widespread interest in benzimidazole-containing structures has prompted extensive studies for their synthesis. There are two general methods for the synthesis of 2-substitued benzimidazoles. One is coupling of o-phenylene diamine and carboxylic acids [41] or their derivatives (nitriles, imidates, or orthoesters) [42], which often require strong acidic condition and temperature. The other way involves a two-step procedure that includes the oxidative cyclohydrogenation of aniline schiff's bases, which are often generated in situ from the condensation of o-phenylene diamine and aldehydes. Various oxidative reagents such as nitrobenzene [43], benzofuroxan [44], 1,4-benzoquinone [45], DDQ [46],

tetracyanoethylene [47], MnO_2 [48], $Pb(OAc)_4$ and $NaHSO_3$ [49] have been employed. In the present study, the syntheses of substituted benzimidazoles have been attempted with clay supported titanium catalyst under conventional heating and microwave irradiated conditions.

6.4.2.1 Synthesis of benzimidazoles

Synthesis of substituted benzimidazoles was carried out by stirring o-phenylene diamine and various substituted benzaldehyde at 50°C and also under microwave irradiation conditions (Scheme 3).

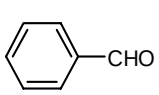
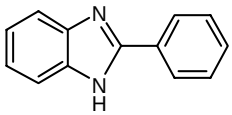
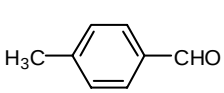
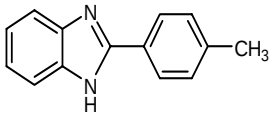
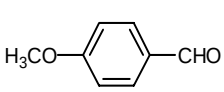
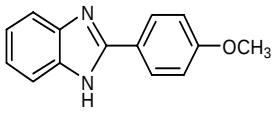
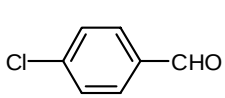
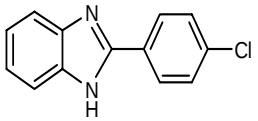
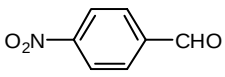
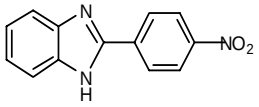
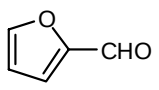
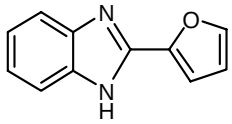
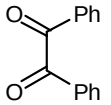
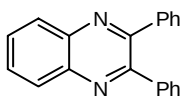


Scheme 3 Synthesis of benzimidazoles using microwave or conventional heating

6.4.2.2 Synthesis of quinoxalines

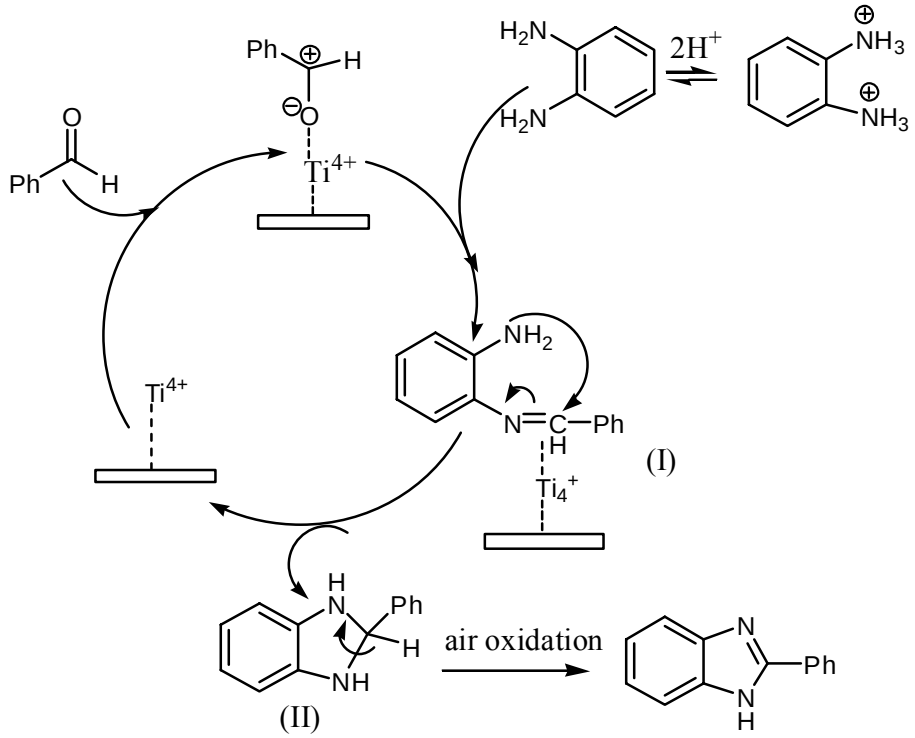
Substituted quinoxaline derivatives exhibit a wide variety of biological activities. It has been reported that some quinoxalines demonstrated antibacterial [55-56], antifungal [57-60], antiviral [61-63], antidepressant [64], hypoglycemic [65], anti-inflammatory [66], excitatory amino acid antagonistic [67] , antiglaucoma [68] antiparasite [69], antituberculosis [70], anticancer [71], and anti HIV-1 [72] activities. The present catalyst is also used for the synthesis quinoxaline. The yield obtained for this condensation is excellent implicating that the catalyst may be used for the synthesis of substituted quinoxalines.

Table 6.5 Synthesis of benzimidazoles and quinoxaline derivatives

Entry	Carbonyl compound	Product	Yield% (time 24 h) Temperature 50°C	Yield% (time min) Microwave
1			79	84(3)
2			74	79(4)
3			62	76(3)
4			82	88(3)
5			71	79(3)
6			68	76(4)
7			91	92(3)

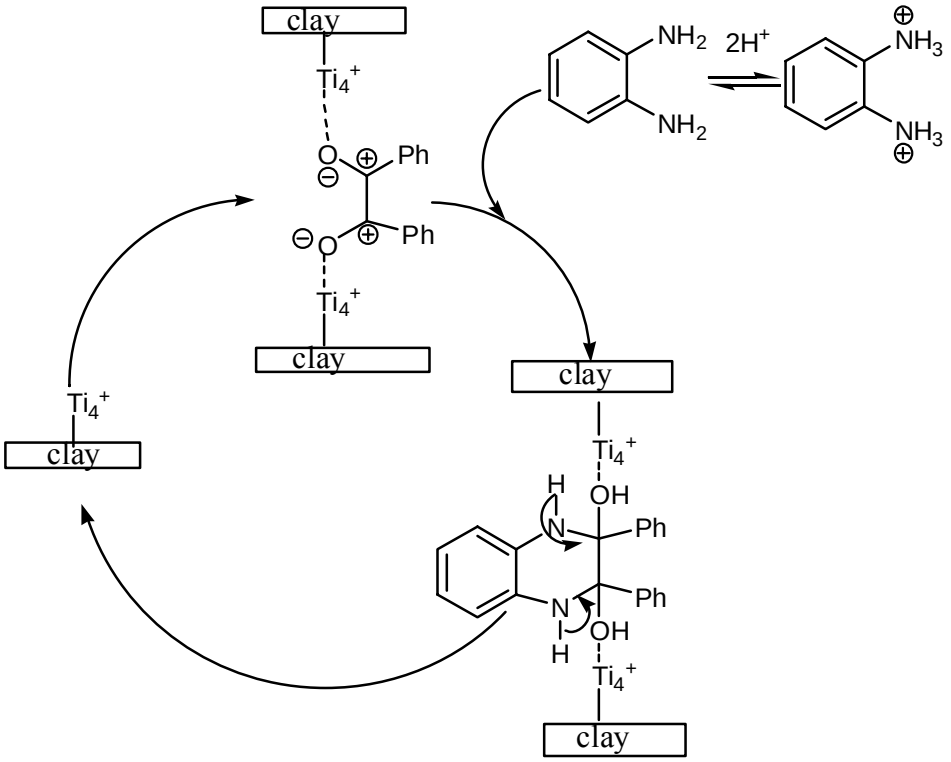
Aldehyde (5 mmol), o-phenylene diamine (5 mmol), K10Ti catalyst (500 mg), 5ml methanol. [a] Isolated yield, MW 360W 3-4min.

The synthesis of substituted benz imidazoles using conventional heating and microwave irradiation conditions were carried out for a series of aldehydes. The advantage of microwave in the synthesis of the title compound was reflected both in yield and time. The results are summarized in table 6.5. The conventional heating required 24h for the completion of the reaction. Microwave condition required 3-4min.



Scheme 4. Proposed mechanism of Titanium catalyst assisted benzimidazole synthesis

The reaction between an aldehyde and a diamine leads to the formation of Schiff base (I) which is stabilized by clay supported Titanium catalyst. Intramolecular attack by the second amino group on C=N double bond facilitates the formation of hydrobenzimidazole (II) which undergoes subsequent air oxidation [50] to give the desired benzimidazole as the final product.



Scheme 5 Proposed mechanism for the synthesis of quinoxalines.

Clay supported titanium catalyst facilitates the formation of quinoxaline derivatives as outlined in the mechanism. 1, 2-diketone was stabilized in the interlayer of clay via interaction with Ti^{4+} by partial polarization of carbonyl group which reacts readily with o-phenylene diamine. The resultant amino-1, 2-diol undergoes base-induced dehydration to give quinoxaline as the end product.

6.4.2.3 Recycling of the catalyst

At the end of the reaction, both conventional and microwave assisted synthesis, the catalyst was filtered, washed with diethyl ether, dried at 130°C for 1h, and reused. The recycling efficiency of the catalyst was checked by selecting benzaldehyde and o-phenylene diamine. The recycled catalyst was

found to be active for three cycles without appreciable loss in catalytic activity. The results are summarized in table 6.6

Table 6.6 Recycling studies of the catalyst

Catalyst	Product	Yield of the product %		
K10Ti	Benzimidazole	First cycle	Second cycle	Third cycle
		80	76	70

Reaction condition: benzaldehyde (5 mmol), o-phenylene diamine (5 mmol), catalyst 500 mg K10Ti, 5 ml methanol, MW= 360W, 5min.

All the products are known compounds and were characterized by comparing IR and ^{1}H NMR spectral data as well as melting points with those reported in the literature. All yields refer to that of isolated pure products.

6.5 Experimental

6.5.1 Synthesis of 2, 4, 6 triarylpyridines. General procedure for conventional heating

A mixture of aldehyde (1mmol), substituted ketone (2 mmol), NH_4OAc (1.3mol %) and activated K10 clay (0.2 g) was stirred at 120^{o}C. The progress of the reaction was monitored by TLC. After the completion of the reaction, hot ethanol was added to the mixture and the insoluble catalyst was filtered off. The pure product was obtained by recrystalisation from the ethanol.

6.5.2 Synthesis of 2, 4, 6-triarylpyridines under microwave heating

Aldehyde (1mmol), ketone (2mmol), ammonium acetate (1.3mol %) and the catalyst 0.2 g were mixed well in a mortar and transferred to a beaker. The mixture was irradiated at 160W for one minute and 360W till the completion of the reaction. The reaction was monitored using TLC (hexane: ethylacetate 9: 1) at one minute interval. After the reaction, hot ethanol was added to the mixture and the insoluble catalyst was filtered off. The pure product was obtained by the slow evaporation of the solvent.

6.5.3 Reusability of the catalyst

At the end of the reaction, both conventional and microwave assisted synthesis, the catalyst was filtered, washed with diethyl ether, dried at 130°C for 1h and reused. The recycled catalyst was found to be active over three cycles without appreciable loss in catalytic activity under both conditions.

All the products are known compounds and were characterized by comparing FT-IR and ^{1}H NMR spectral data as well as melting points with those reported in the literature. All yields refer to that of isolated pure products.

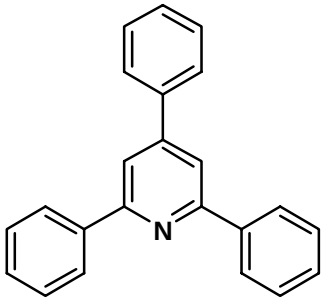
6.5.4 Synthesis of substituted benzimidazoles or quinoxalines under conventional heating

A mixture of aldehyde (5 mmol), o-phenylene diamine (5 mmol), and activated K10Ti clay catalyst (0.5 g) was stirred at 50°C. The progress of the reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was washed with water, extracted with dichloromethane (20 ml), filtered and dried with anhydrous sodium sulphate. The crude products were recrystallised from ethyl acetate.

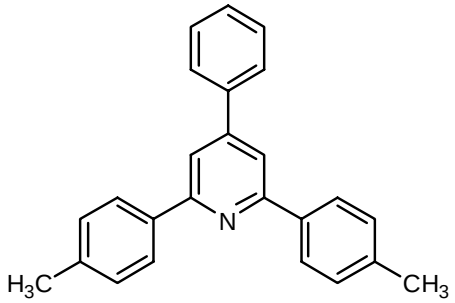
6.5.5 Synthesis of substituted benzimidazoles or quinoxalines under microwave heating

A mixture of aldehyde (5 mmol), o-phenylene diamine (5 mmol), and activated K10Ti clay catalyst (0.5 g) was mixed thoroughly in a mortar using 5 ml methanol. The mixture was irradiated at 160W for one minute and 360W till the completion of the reaction. The reaction was monitored using TLC (hexane: ethylacetate 9: 1) at one minute interval. After the completion of the reaction, the reaction mixture was extracted with dichloromethane (20 ml), filtered, washed with water and dried with anhydrous sodium sulphate. The products were recrystallised from ethyl acetate.

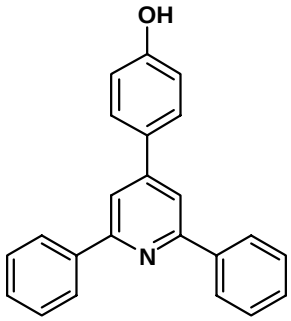
Characterisation data of selected products



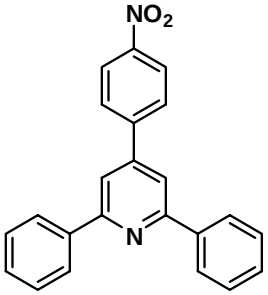
2, 4, 6-triphenylpyridine (Entry 1). Mp 130–132°C; ^{1}H NMR ($CDCl_3$, 400MH_Z): δ 7.42–8.22 (m, 17H), LC-MS (m/z): 308.1 (M+1). FT-IR (KBr): 3032, 1604, 1544, 1232, 1025 cm^{-1}.



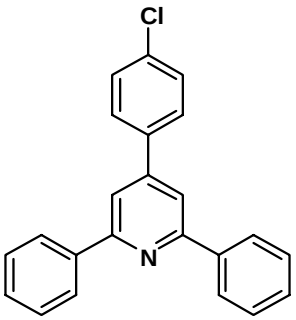
4-phenyl-2, 6-di*p*-tolylpyridine (Entry 2) Mp 156-158°C ^{1}H NMR ($CDCl_3$, 400MH_Z): δ 7.22–8.21 (m, 15H), 2.43 (s, 6H), LC-MS (m/z): 336.2 (M+1). FT-IR (KBr): 3030, 1654, 1593, 1330, 1180cm^{-1}.



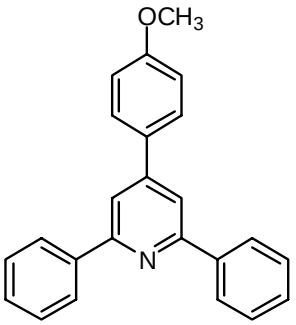
4-(2, 6-diphenylpyridin-4-yl) phenol (Entry 4). Mp 197°C; ^{1}H NMR ($CDCl_3$, 400MH_Z): δ 8.20 (dd, 4H, J=1.2Hz), 7.85 (s, 2H), 7.68(d, 2H, J=4.4Hz), 7.43-7.68(m, 6H), 6.99(d, 2H, J=8.4H_Z), 4.99(s, 1H) LC-MS (m/z): 324.3 (M+1). FT-IR (KBr): 3038, 1598, 1517, 1602, 1207, 1109 cm^{-1}.



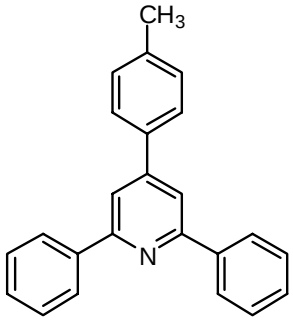
4-(4-nitrophenyl)-2, 6-diphenylpyridine (Entry 5). Mp 203-205 °C; ^{1}H NMR ($CDCl_3$, 400MH_Z): δ 7.42–7.89 (m, 16H), LC-MS (m/z): 353.3 (M+1). FT-IR (KBr): 3069, 1608, 1528, 1351, 1218cm^{-1}.



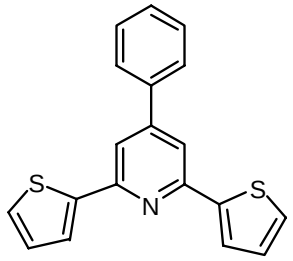
4-(4-chlorophenyl)-2, 6-diphenylpyridine (Entry6). Mp 118-119°C; ^{1}H NMR ($CDCl_3$, 400MH_Z): δ 7.45-8.20 (m, 16H) LC-MS (m/z): 342.8(M+1).FT-IR (KBr): 3023, 1656, 1600, 1334, 1222 cm^{-1}.



4-(4-methoxyphenyl)-2, 6-diphenylpyridine (Entry 8). Mp 101-102°C; ^{1}H NMR ($CDCl_3$, 400MH_Z): δ 7.42-8.23 (m, 16H) 3.73(s, 3H) LC-MS (m/z): 338.2(M+1). FT-IR (KBr): 2998, 1650, 1600, 1338, 1280 cm^{-1}.

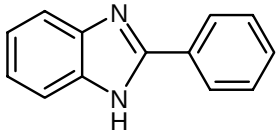


2,6-diphenyl-4-p-tolylpyridine(Entry 9) Mp 116-118°C; ^{1}H NMR ($CDCl_3$, 400MH_Z): δ 7.21-8.23 (m, 16H), 2.51(s, 3H) LC-MS (m/z): 322.4(M+1).FT-IR (KBr): 3020, 1655, 1605, 1330, 1025 cm^{-1}.

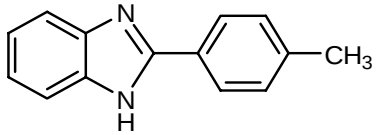


4-phenyl-2,6-di(thiophen-2-yl)pyridine (Entry 14) Mp 168-170°C; ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.40-8.24 (m, 7H), 7.1(m,1H), 7.41(m, 1H), 7.61(m, 1H). LC-MS (m/z): 320.8(M+1). FT-IR (KBr): 3023, 1656, 1600, 1334, 1222 cm^{-1}.

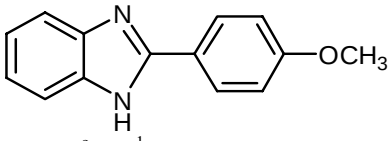
Benzimidazoles and Quinoxalines



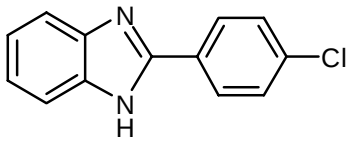
Mp: 294°C (lit.,[51] 295); ^{1}H-NMR(400MHz, $CDCl_3$) δ(ppm) 8.17-8.21(m,2H),7.62(dd, 2H, J=8, 3.2 Hz), 7.21-7.65(m, 5H),4.91 (s,1H).



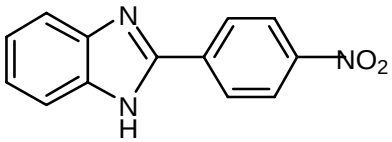
Mp: 294°C (lit.,[52] 295); ^{1}H-NMR(400MHz, $CDCl_3$) δ(ppm) 8.06 (d, 2H, J=8.2Hz),7.61(m, 2H, J=8. 2 Hz), 7.29 (d, 2H, J=7.6Hz),7.18-7.27(m,2H) 4.71(s,1H), 2.40(s,3H).



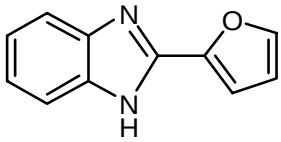
Mp: 224°C (lit.,[53] 226-227°C); ^{1}H-NMR(400MHz, $CDCl_3$) δ(ppm) 7.46(d, 2H, J=7.4Hz), 7.02-7.24(m, 4H), 6.60(d, 2H, J= 7.8Hz) 4.62(s,1H), 3.73(s, 3H).



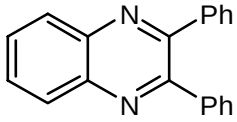
Mp: 289°C (lit.,[53] 294°C); ^{1}H-NMR(400MHz, $CDCl_3$) δ(ppm) 8.18(d, 2H, J=8.4Hz), 7.45(d, 2H, J=8.4Hz) 7.19-7.25(m, 2H), 6.62(d,2H J=7.8Hz) 4.67(s,1H).



Mp: 314°C (lit.,[53] 316°C); ^{1}H-NMR(400MHz, $CDCl_3$) δ(ppm) 8.15-8.22(m, 2H),7.16-7.23(m,2H), 6.7-6.9(m,4H), 4.4(s,1H).



Mp: 287°C (lit.,[53] 287°C); ^{1}H-NMR(400MHz, $CDCl_3$) δ(ppm) 7.31-7.32(m,1 H), 7.22-7.36(m, 4H), 6.90-7.10(m,1H), 6.10-6.20(m,1H), 2.91(s,1H).



Mp: 122°C (lit.,[54] 122°C); ^{1}H-NMR(400MHz, $CDCl_3$) δ(ppm) 8.16 (dd,2H, J=3.4, 6.30Hz),7.77(dd,2H, J=3.4, 6.3Hz),7.75(dd, 2H, J=3.4, 6.3Hz), 7.52(m, 4H), 7.37(m, 6H)

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Chapter 7

SUMMARY AND CONCLUSIONS

Contents

Basic research in catalysed organic synthesis promises a breakthrough that may revolutionize the industries in future by developing new catalysts. The current and future chemists are trying to mitigate environmental problems by replacing hazardous catalysts by safe one. The goal of a catalyst researcher is to produce and reproduce a commercial product, which can be used as a stable, active and selective catalyst. Continuous efforts of chemists are to develop environmentally friendly catalysts with minimal or no environmentally unfriendly by-products. Development of novel catalyst systems which are environmentally friendly and cheap that facilitates some industrially important reactions should be of great importance. The major objectives of the present work consisted of preparation of different metal containing clay catalysts, characterization and their application in various organic reactions. Some reactions were carried out under solvent free conditions and microwave assisted conditions, which are synthetically important. This chapter deals with the summary and conclusions of the results of the present work and the scope for further research in organic synthesis mediated by heterogeneous clay catalysts.

7.1 Introduction

Catalysis is an active field both in academic and industrial research. It renders better form of life by offering efficient reactions in various industries in terms of energy consumption and waste production. The basic principle of

catalysis is: catalytically active species reacts with the substrates of a reaction forming reactive intermediates coordinated to the active sites. The activation energy of the reaction is lowered during these processes and product formation occurs at low energy with regeneration of the catalyst. Different forms of clays such as natural clays, synthetic clays, pillared calys and ion exchanged clays are being used as heterogeneous catalysts in many organic reactions.

The prime intension of the present work was a synthetic investigation of the preparation, properties and catalytic activity of some modified clay catalysts. Different methods were adopted for the preparation of catalysts such as wet impregnation, pillaring, ion exchange, etc. The structure and reactivity of the prepared catalysts could be understood from the characterization data of the catalysts. The catalytic activity of these catalysts was studied by employing them in different reactions which are synthetically and industrially important. The thesis is dedicated to the utilization of different methods of modification of clays giving emphasis to synthetic applications, preparation and characterization.

7.2 Summary

The chapter wise organization of the thesis is as follows

Chapter 1 has presented an introduction to clays, structure and classification. A detailed description of various methods of modification of clays for the use as catalysts was also presented. Literature survey of clay as catalysts in organic reactions such as condensation, addition, substitution, rearrangement and oxidation reactions was presented. Materials and methods used in this work was also given in this chapter.

In chapter 2 the preparation of clay supported titanium catalyst, characterization of the catalyst and application of this catalyst for the solvent free synthesis of tetrasubstituted imidazoles have been dealt with. The mechanism of formation of imidazoles and the role of catalyst are discussed. A theoretical

description of substitution effects on the formation of imidazoles by designing isodesmic reactions was also given. The same catalyst was employed for carrying out Mannich reaction, reaction conditions and mechanism were discussed.

In chapter 3, the method of Al-pillaring of natural saponite and its characterization was explained. The catalyst was found to be active for the synthesis of cyclic acetals of pentaerithritol. The mechanism of formation of cyclic acetal and effects of various factors controlling the reaction were studied. The recycling studies of the catalyst were also conducted.

Chapter 4 has focused on the preparation of Cu-Pd KSF and Co-Pd KSF bimetallic catalysts, their preparation, characterization and applications. The Cu-Pd bimetallic catalyst was found to be active for Heck and Suzuki coupling reaction. Plausible mechanisms have been drawn out in each case based on the experimental observations.

Chapter 5 has discussed the preparation of clay supported chiral dipeptide metal complexes of copper and titanium as catalysts. The preparation of catalysts and their characterization have been discussed in the first part of the chapter. Synthesis of furo[3,2,c]quinolines, and pyro[3,2,c]quinolines were achieved in good yield and excellent enatiomeric excess. The influence of various reaction conditions on the catalytic activity was subjected to investigation.

Chapter 6 has described the solvent free synthesis and microwave assisted synthesis of few heterocycles. Montmorillonite K10 and Titanium supported K10 were employed for these reactions. Synthesis of triarylpyridines under solvent free conditions and microwave assisted conditions were tried. Influence of various reaction conditions such as substrate, nitrogen source and catalyst loading were studied for triarylpyridines. Titanium supported K10 was employed for the synthesis of benzimidazoles and quinoxaline. Plausible mechanisms have been drawn out in each case. Effect of substituents on the

substrates was studied by utilizing various aldehydes. A comparison of solvent free and microwave assisted conditions was also discussed.

Chapter 7 presents the summary of important results and future prospects of the present work.

7.3 Conclusions

The major conclusions that can be drawn from the present work are the following

1) Titanium supported Montmorillonite K10 clay catalyst was found to be an efficient catalyst for the solvent free synthesis of tetra substituted imidazoles. Theoretical studies revealed that heat of formation of substituted imidazoles could be calculated designing suitable isodesmic reactions, which could be correlated with the yield of the products.

2) Titanium supported Montmorillonite K10 clay catalyst could also be used for the synthesis of Mannich bases.

3) Al-pillared saponite clay catalyst was found to be an effective catalyst for the synthesis of cyclic diacetals. Aluminium pillaring has enhanced the surface area, pore volume and total acidity. Elemental and morphological characterization of the catalyst has revealed that the catalyst was suitable for diffusion controlled reaction because it had a d spacing of 18.4^0A

4) Cu-Pd bimetallic catalyst supported on Montmorillonite K10 clay has given excellent results in Suzuki coupling and Heck coupling reactions. Bimetallic catalyst was found to be better than monometallic catalyst. The characterization of the catalyst has confirmed the presence of Cu and Pd in the catalyst system and two electron redox process was the key factor for enhanced activity.

5) Clay supported dipeptide metal complexes of copper and titanium have been found to be efficient catalysts for the synthesis of furo [3, 2, c] quinolines and pyro [3, 2, c] quinolines. Copper dipeptide complex supported on clays were found to be a better catalyst than titanium catalyst for Aza Diels Alder reaction.

6) Montmorillonite K10 was found to be an efficient catalyst for the solvent free synthesis of triarylpyridines under conventional and microwave conditions. Montmorillonite K10 supported Ti catalyst gave good results in the synthesis of benzimidazoles and quinoxaline.

Different catalysts prepared and the various reactions in which they are employed are summarized in Table 7.1

Table 7.1 Clay catalysed reactions

	Name of reaction	**Catalyst**	**Best activity catalyst**
1	Tetra substituted imidazole synthesis	K10Ti, KSFTi,	K10Ti
2	Mannich reaction	K10Ti, KSFTi, K10Co, K10 Cu,	K10Ti
3	Acetal formation reaction	Natural saponite, pillared saponite, K10	Pillared saponite
3	Biginelli reaction	K10Ti, KSFTi, K10Co, K10 Cu,	KSF Ti
4	Suzuki coupling and Heck coupling reaction	Co-Pd KSF, Cu-Pd KSF	Cu-Pd KSF
5	Aza- Diels Alder reaction	Cu-dipeptide catalyst, Ti-dip catalyst,	Cu-dipeptide catalyst
6	Microwave assisted and conventional synthesis of tri arylpyridine	K10 Clay	K10 clay
7	Aldol condensation	K10 Cu	K10Cu
8	Oxidation of secondary alcohols	K10Ti, KSFTi, K10Cu	K10 Ti
9	Microwave assisted and conventional synthesis Benz-imidazole	K10Ti, KSFTi, KSF, K10, K10Cu	K10Ti

7.4 Future outlook

Catalysis is a technologically important field which determines the quality of life in future. Catalyst research in pharmaceutical industry, fine chemical synthesis and emission control demands supported catalysts in bulk quantities. In the present work it was observed that clay supported catalysts mentioned in various chapters could also be used for the synthesis of similar molecules. The K10Ti catalyst can be used for the synthesis similar substituted imidazole derivatives under solvent free conditions and synthetically important Mannich bases of substrates containing various substituents. Al-pillared saponite can be used for acetalation of other polyhydroxy compounds like glycerol, mannitol etc. Cu-Pd KSF catalyst has found application in C-C bond forming reactions which can be applied to other reactions and similar methods can be adopted for the synthesis of other catalysts by changing the transition metals. Montmorillonite K10 catalysed synthesis of triarylpyridines can be extended to the synthesis tetrasubstuted pyroles. K10Ti can also be utilized for the synthesis of similar heterocycles.