

**SELECTIVE LIQUID PHASE ALCOHOL OXIDATION AND  
HECK-TYPE COUPLING REACTIONS USING  
HETEROGENEOUS CATALYSTS**

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**BY**

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## CERTIFICATE

This is to certify that the work incorporated in the thesis, **“Selective Liquid Phase Alcohol Oxidation and Heck-type Coupling Reactions Using Heterogeneous Catalysts”** submitted by Deepa K. Dumbre, for the Degree of Doctor of Philosophy, was carried out by the candidate under our supervision in the Organic Chemistry Division and Chemical Engineering & Process Development Division, National Chemical Laboratory, Pune – 411 008, India. Such material as obtained from other sources has been duly acknowledged in the thesis.

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## **DECLARATION**

I hereby declare that the thesis “**Selective Liquid Phase Alcohol Oxidation and Heck-type Coupling Reactions Using Heterogeneous Catalysts**” submitted for the degree of Doctor of Philosophy to the University of Pune has not been submitted by me for a degree to any other University.

**Deepa K. Dumbre**

*Dedicated to*

*my*

*Parents*

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## Summary and Conclusions

There is no universal definition of the fine chemicals, but from the chemical point of view generally accepted definition is the building blocks and performance molecules with multifunctional groups, many possible isomers with low volatility and limited thermal stability and hence its formation requires mild reaction conditions. Fine chemicals, including medicinal and pharmaceuticals, are specialized products that were first manufactured in local drugstores as early as the late 19th century.

Green chemistry is defined as environmentally benign chemical synthesis. The synthetic pathways are designed in such a way that there is least pollution to the environment which pollute the atmosphere or eliminate the use and generation of hazardous substances. The green chemistry seeks to reduce and prevent pollution at its source. The reaction or the synthesis is considered to be green if there is maximum incorporation of the starting materials and reagents in the final product.

The synthesis of fine chemicals using conventional homogeneous catalysts poses several problems, such as difficulties in its separation and recovery, disposal of spent catalyst, formation of undesirable and/or toxic wastes, etc. Worldwide efforts have been made for replacing homogeneous catalysts by easily separable and reusable heterogeneous catalysts. Heterogeneous solid catalysts have advantages, such as their easy recovery (or separation), reusability, and much lower toxicity. The separation of solid catalyst from reactant and product usually involves simple filtration or centrifugation. Hence, the heterogeneous solid catalysts are environmentally much more benign.

The oxidation of alcohols into aldehydes is an important transformation in organic synthesis and numerous oxidizing agents (viz. organic peroxides,  $\text{H}_2\text{O}_2$  and molecular oxygen) are used to effect this key reaction. Selective oxidation of benzyl alcohol to benzaldehyde is a practically important reaction for the production of chlorine-free benzaldehyde required in

chemical and pharmaceutical industries like perfumery, pesticides and agrochemical industries. The vapor-phase oxidation of benzyl alcohol suffers from the drawback of formation of carbon oxides leading to significant carbon loss. Therefore, liquid-phase oxidation of benzyl alcohol to benzaldehyde is preferable. In the past, efforts have been made to produce benzaldehyde by oxidizing the methylene group using stoichiometric quantities of oxidizing agents e.g.  $\text{KMnO}_4$  and  $\text{CrO}_3$ . These stoichiometric reactions have several limitations, such as the formation of a large amount of liquid and solid wastes and corrosive nature of the acidic reaction medium.

However, benzaldehyde can also be produced by the liquid phase oxidation of benzyl alcohol by TBHP using transition metal (viz. Co, Mn, Cu, or Fe) compounds as catalyst. For developing the chlorine-free benzaldehyde, it is necessary to have a non-toxic and reusable solid catalyst, which shows high activity and selectivity in the oxidation of benzyl alcohol to benzaldehyde by TBHP in the absence of any solvent and also without significant leaching of its components in the liquid reaction mixture. It is therefore, interesting to explore the possibility of using  $\text{MnO}_4^-$ -exchanged Mg-Al-hydrotalcite and supported nano-gold catalyst for the selective oxidation of benzyl alcohol to benzaldehyde, using TBHP as an oxidizing agent.

Heck reaction is an important tool for generating the C-C bond formation between aryl halides and olefins catalyzed by supported palladium catalyst in the presence of a base. It has very important applications in synthetic organic chemistry to a variety of molecules.

The other important reaction for the C-C bond formation between aryl halide in the presence of finely divided copper at higher temperature is Ullmann reaction. The traditional version of the Ullmann reaction requires harsh reaction conditions, with erratic yields. Since its discovery introduced some improvements and alternative procedures for C-C bond formation reaction. However, C-C bond formation can also be produced by using supported palladium catalyst, with good yields for industrial applications.

The work for the Ph.D. thesis was undertaken as a part of the comprehensive R & D programme in our laboratory (NCL, Pune) for replacing conventional homogeneous catalysts by novel, reusable and highly active/selective heterogeneous catalysts for the synthesis of fine chemicals by environmentally benign/green processes.

The thesis has been divided into six chapters, as follows:

## **Chapter 1: Introduction – Literature Survey, Objectives and Scope**

In this chapter, a general introduction including background and literature survey, covering

- Oxidation of benzyl alcohol to benzaldehyde, using  $\text{MnO}_4^-$ -exchanged Mg-Al-HT, LDH and supported nano-gold catalysts.
- Heck reaction of aryl halides using various supported palladium catalysts.
- Ullman reaction for biphenyl formation using supported palladium catalysts.

And also the objectives/scope of the Ph.D work has been presented.

## **Chapter 2: Experimental**

In this chapter, the experimental procedures for

- the preparation and/or modification of  $\text{MnO}_4^-$ -exchanged Mg-Al-HT, LDH catalysts, supported nano-gold catalysts and supported Pd catalysts.
- the characterization of the catalysts by different surface and bulk analytical tools (viz. XRD, XPS, TEM, ICP)
- the oxidation of benzyl alcohol to benzaldehyde by TBHP in absence of solvent
- the Heck reaction of aryl halide for C-C bond formation
- the Ullmann reaction for biphenyl formation

have been described.

### **Chapter 3: Solvent-free Selective Oxidation of Benzyl Alcohol by TBHP Benzaldehyde using Solid Catalysts derived from Hydrotalcite, Layered Double Hydroxides or Mixed Metal Hydroxides**

This chapter deals with the detailed study of the influence of hydrotalcite and layered double hydroxide catalysts in the oxidation reaction of benzyl alcohol. Among the  $\text{MnO}_4^-$ -exchanged Mg-Al-hydrotalcites (Mg/Al=2-10) ratio, the Mg/Al=10 was found to be highly active, selective, stable and reusable catalyst for the liquid phase oxidation of benzyl alcohol to benzaldehydes by TBHP in the absence of any solvent. The oxidation reaction catalyzed by this catalyst is truly heterogeneous; without leaching of the exchanged  $\text{MnO}_4^-$  anions. The oxidation activity,  $\text{H}_2\text{O}_2$  decomposition activity and basicity of the catalyst are increased with increasing the Mg/Al ratio in the hydrotalcite, indicating a good correlation among them. The thermal stability of the hydrotalcite increased after the exchanging the  $\text{MnO}_4^-$  anions. The performance of the catalyst is markedly improved in its subsequent reuse in the oxidation reactions probably due to the removal of moisture from the catalyst.

Among the transition metals (Co-Al, Ni-Al, Zn-Al, Mg-Fe, Mn-Fe, Co-Fe, Ni-Fe, Zn-Fe, Mg-Cr, Mn-Cr, Co-Cr, Ni-Cr, Zn-Cr and Cu-Cr) containing layered double hydroxides (LDH) and/or mixed hydroxides, the Mn, Co and Cu and Zn-Cr containing LDH and/or mixed hydroxides are promising catalysts for the solvent-free liquid-phase oxidation of benzyl alcohol to benzaldehyde.

### **Chapter 4: Solvent-free Selective Oxidation of Benzyl Alcohol by TBHP to Benzaldehyde using supported nano-gold Catalysts**

This chapter deals with the detailed study of the influence of supported nano-gold catalysts in the oxidation reaction of benzyl alcohol. Among the different methods of preparation of gold deposition on support are mainly impregnation, deposition-precipitation (DP), co-precipitation (CP) and homogeneous-deposition-precipitation (HDP). The catalyst

prepared by the HDP method showed the best performance in the benzyl alcohol to benzaldehyde oxidation by TBHP in absence of any solvent.

Among the supported gold catalysts, prepared by the HDP method, the Au/MgO, Au/TiO<sub>2</sub> and Au/U<sub>3</sub>O<sub>8</sub> showed the best performance in the oxidation reaction of benzyl alcohol by TBHP and is strongly influenced by gold loading, method of preparation and catalyst calcination temperature, reaction time and reaction temperature parameters. The observed higher catalytic activity of the HDP catalyst as compared to that of DP catalyst was expected because of its higher Au loading; lower Au particle size and/or higher surface Au<sup>3+</sup>/Au<sup>0</sup> ratio.

There is no direct relationship exists between the surface properties of the metal oxide supports and the gold loading in the supported metal oxide catalysts prepared by the HDP method. However, the particle size of the gold deposited on the metal oxides is found to be decreased with increasing the surface area of the support used in the catalyst.

## **Chapter 5: C-C coupling by the Heck Reaction using Heterogeneous Catalysts**

This chapter deals with the detailed study of the influence of supported palladium catalysts on the Heck reaction of aryl halides. The different methods of preparation of Pd deposition on support are mainly impregnation, deposition-precipitation (DP), co-precipitation (CP) and homogeneous-deposition-precipitation (HDP). The catalyst prepared by the impregnation method showed the best performance in the Heck reaction of aryl halides and styrenes. The reaction is strongly affected by method of preparation, reaction time and reaction temperature parameters. The scope for the future work along with conclusions has also been discussed.

Among the various support (viz. Al<sub>2</sub>O<sub>3</sub>, CeO<sub>2</sub>, ZrO<sub>2</sub>, MgO), prepared by impregnation method and followed by reduction with hydrazine, Pd/zirconia showed excellent results in the

Heck reaction of aryl halides. However, the support plays an important role in deciding the performance of the catalyst.

The observed higher catalytic activity of the impregnation catalyst as compared to that other catalyst was expected because of its higher palladium loading on the support surface, thus providing higher active sites and higher palladium particle size. It is interesting to note that the catalyst performance, particularly the product yield, the catalyst showed reusability without significant decrease in the yield.

## **Chapter 6: C-C coupling by the Ullmann reaction using Heterogeneous Catalysts**

This chapter deals with the detailed study of the influence of supported palladium catalysts on the Ullmann reaction of aryl iodides for the formation of biphenyl. The different methods of preparation of Pd deposition on zirconia are mainly impregnation, DP, CP and HDP. The catalyst prepared by the impregnation method showed the best performance in the Ullmann reaction of aryl iodides. The reaction was studied for general observations like method of preparation, reaction time and reaction temperature parameters. The scope for the future work along with conclusions has also been discussed.

However, the catalyst performance, particularly the product yield, the catalyst showed reusability without significant decrease in the yield and the biphenyls were obtained in good yields.

## **CHAPTER-1**

**INTRODUCTION - LITERATURE SURVEY,**

**OBJECTIVES AND SCOPE**

# CHAPTER-1

## INTRODUCTION – LITERATURE SURVEY, OBJECTIVES

### AND SCOPE

#### 1.1 FINE CHEMICALS GENERAL

There is no universal definition of fine chemicals, but from the chemical point of view generally accepted definition is that they are the building blocks and performance molecules with multifunctional groups, many possible isomers with low volatility and limited thermal stability and hence their formation requires mild reaction conditions.

Compared to basic chemicals, fine chemicals are relatively small-scale but high-value products with high purity requirements, traditionally produced *via* multistep non-catalytic synthesis in batch equipment. Hence the development of fine chemical synthesis needs processes, which may be used on a broader scale with a scope of implementation in multipurpose equipments.

Fine chemicals, including medicinals and pharmaceuticals, are specialized products; they were first manufactured in local drugstores as early as the late 19th century. For pharmaceuticals in particular, the time for development of the production process is often very short since ‘time to market’ can significantly affect the profitability of a new drug. Owing to a growing emphasis on production cost and waste minimization, even for high-value life science chemicals, there is an increase in the application of catalytic methods, which has been promoted by the development of corresponding technologies in the fine chemical synthesis.

##### 1.1.1 Principles of Green Chemistry

Green chemistry is defined as environmentally benign chemical synthesis. The synthetic schemes are designed in such a way that there is least pollution to the environment which pollute the atmosphere or eliminate the use and generation of hazardous substances,



and green chemistry seeks to reduce and prevent pollution at its source. In 1990, the pollution prevention act was passed in the United States. This act helped for dealing with pollution in an original and innovative way.

Paul Anastas, then of the environmental protection agency, and John C. Warner developed 12 principles of green chemistry [1], which help to explain what the definition means in practice. The principles cover such concepts as:

- the design of processes to maximize the amount of raw material that ends up in the product;
- the use of safe, environment-benign solvents and starting materials where possible;
- the design of energy efficient processes;
- the best form of waste disposal, aiming not to create it in the first place;
- the use of catalysts should be preferred whenever possible.

The reaction or the synthesis is considered to be green if there is maximum incorporation of the starting materials and reagents in the final product. The concept of atom economy developed by B. M. Trost [2] is a consideration of ‘how much of the reactants end up in the final product’. The same concept determined by R. A. Sheldon [3]. With these concepts and advancement of science, green chemistry has changed our life style.

### **1.1.2 Homogeneous versus Heterogeneous Catalysis**

Catalytic reactions are mainly classified into two broad categories – homogeneous and heterogeneous catalysis but these both categories have their limitations and advantages. The major limitations of homogeneous catalyst are, they are usually difficult to reuse, difficulties in their separation and disposal and also their high toxicity.

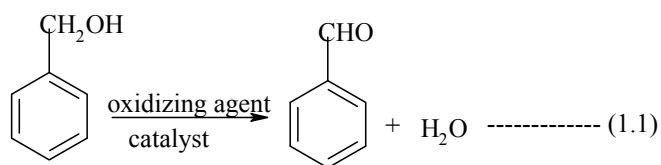
Heterogeneous solid catalysts have advantages, such as their easy recovery (or separation), reusability, and much lower toxicity. The separation of solid catalyst from

reactant and product usually involves simple filtration or centrifugation. Hence, the heterogeneous solid catalysts are environmentally much more benign as well as economical.

## 1.2 HETEROGENEOUSLY CATALYZED LIQUID-PHASE REACTIONS FOR SYNTHESIS OF FINE CHEMICALS

### 1.2.1 Oxidation of Benzyl Alcohol

The oxidation of alcohols into aldehydes is an important transformation in organic chemistry and numerous oxidizing agents (viz. organic peroxides, H<sub>2</sub>O<sub>2</sub> and molecular oxygen) are used to effect this key reaction. Selective oxidation of benzyl alcohol to benzaldehyde (reaction 1.1) is a practically important reaction for the production of chlorine-free benzaldehyde required in chemical and pharmaceutical industries like perfumery, pesticides and agrochemical industries.



A number of studies on the oxidation of benzyl alcohol to benzaldehyde using various oxidizing agents over a variety of solid catalysts have been reported in the literature.

Vapor-phase oxidation of benzyl alcohol [4-14] suffers from the drawback of formation of carbon oxides leading to significant carbon loss. Therefore, liquid-phase oxidation of benzyl alcohol to benzaldehyde is preferable. A number of catalysts viz. PTC (phase transfer catalyst) [15-18], catalyst containing different metals such as Pt [19], Ru [20-23], Pd [24-35], Cu [36,37], hypervalent iodine [38], Ni-Al-HT [39], Nitroxyl radical [40], MnO<sub>2</sub> [41], Mn-Cu [42], Au/Fe<sub>2</sub>O<sub>3</sub> [43], and n-hydroxyphthalimide as a co-oxidant [44] are reported in literature for benzyl alcohol oxidation. Recently, Choudhary et. al. [45-

49] has reported different hydrotalcite,  $\text{MnO}_4^{-1}$ -exchanged hydrotalcite and supported gold catalysts as active and highly selective catalysts for the benzyl alcohol oxidation using aqueous TBHP/molecular oxygen as an oxidant. Then recently, there is report on photocatalytic oxidation of benzyl alcohol by 9-phenyl-10-methylacridinium [50] and by an artificial enzyme [51].

The above literature review clearly tells us that though several studies have been performed on the liquid phase oxidation of benzyl alcohol to benzaldehyde, there is enough scope for developing a novel solid catalyst for the selective oxidation of benzyl alcohol to benzaldehyde using *tert*-butyl hydroperoxide as the choice of oxidant. A number of different oxidants have been used for oxidation of alcohols and these oxidants include peracids, organic hydroperoxide, hydrogen peroxide and molecular oxygen. The choice of oxidant basically depends on two factors; (1) the nature of the corresponding by-product and (2) the active-oxygen content in the oxidant (besides price and ease of handling). The former factor is most important for environmental reasons, while the later one influences the productivity of the process.

However, among all the oxidizing agents, molecular oxygen is the most attractive option, but its much lower reactivity restricts its applicability to high temperature reactions. Apart from this,  $\text{O}_2$ /organic vapour mixtures may sometimes spontaneously ignite, leading to explosion hazards. An aqueous  $\text{H}_2\text{O}_2$  is another attractive option since it is versatile oxidizing agent, producing water (which is environmentally benign) as the only by-product. However, the inherent co-production of water poses some serious difficulties, because most of the transition metal based catalysts are very sensitive to water. It may cause leaching of their active metal component from the catalyst and also have retarding effect on some reactions.

For catalytic liquid phase oxidation, organic hydroperoxides are commonly used as an oxidant. The hydroperoxides are, however, more expensive and the active oxygen component in them is rather low. Their use generates stoichiometric amounts of corresponding alcohols, which can be removed easily by simple distillation and reduces the alcohol to low residual levels. The generated alcohol is used as a solvent, as a denaturant for ethanol, as an ingredient in paint removers, as an octane booster for gasoline, as an oxygenate gasoline additive, and as an intermediate in the synthesis of other chemical commodities such as flavors and perfumes. However being a tertiary alcohol, this tert-butanol (which is generated from TBHP) is more stable to oxidation and less reactive than the other isomers of butanol. This makes the search for a new environmentally friendly, effective oxidation catalytic system, which is demanding and challenging one.

A number of studies have been reported for the oxidation of benzyl alcohol to benzaldehyde using different catalysts and/or oxidizing agents.

These studies are summarized in Table 1.1.

**Table 1.1** Summary of work on the liquid-phase oxidation of benzyl alcohol to benzaldehyde

Catalyst	Oxidizing agent	Reaction condition		Conversion (%) (Selectivity %)	Remarks	Investigator (Year)	Ref.
		Temp.	Reaction mixture				
I	II	III	IV	V	VI	VII	VIII
Phase transfer catalysts with catalytic amounts of aqueous hypochlorite.	NaOCl	RT	Alcohol (0.01 mol), 2-chloronaphthalene (0.87 g, used as internal GC standard), tetrabutylammonium bisulphate ( $5.4 \times 10^{-4}$ mol), 25 ml $\text{CH}_2\text{Cl}_2$ , sodium hypochlorite (0.04 mol)	77 (76) 49 (47) 89 (79) 82 (78) 100 (100) 99 (92) 98 (94)	PTC with aqueous NaOCl is extremely effective, inexpensive and readily available reagent equal or even superior to more exotic oxidants for the oxidation of alcohols.	Lee et. al (1976)	15
Phase transfer catalyst (TOMA)-Electron transfer catalyst (TPPMn)	NaOCl	RT	Alcohol (2 mmol), TPP.Mn (III) Cl (0.007mmol), TOMA (0.12 mmol), NaOCl (0.36 mmol), $\text{CH}_2\text{Cl}_2$ - $\text{H}_2\text{O}$ (3 ml/2 ml)	88 (-) 94 (-) 57 (-)	Direct oxidation of benzyl alcohol by NaOCl was very slow, greatly enhanced by phase transfer catalyst, TOMA and by an electron transfer catalyst, TPPMn.	Tabushi et. al (1979)	16
Hypochlorite+ PTC	Hypochlorite	30 °C	Alcohol ( $0.926\text{Kmmol/m}^3$ , PTC ( $0.01\text{Kmmol/m}^3$ ), Toluene	90 (100)	The optimum conditions are obtained with CTMAB as PTC and toluene as the best solvent.	Asai et. al (1994)	17
Heteropolyacids and Phase transfer catalyst	$\text{H}_2\text{O}_2$	RT	Alcohol, $\text{CCl}_4$ , heteropolyacid, 1 ml $\text{H}_2\text{O}$	-	A detailed investigation has been carried out on the use of heteropolyacids in conjunction with PTC in the oxidation of benzyl alcohol to Benzaldehyde. Dodeca-tunstophosphoric acid (WPA) and cetyl trimethylammonium bromide was found to be the most effective co-catalyst and the best phase transfer catalyst, respectively exhibiting highest catalytic activity.	Yadav et. al (2001)	18
$\text{PtO}_2$	Air	RT	Alcohol, Pt (by the reduction of $\text{PtO}_2$ by $\text{H}_2$ )	72 (100)	Benzaldehyde was obtained selectively in good yield.	Sneed et. al (1954)	19

**Table 1.1** (continued)

I	II	III	IV	V	VI	VII	VIII
Ru-Co-Al-hydroxalcite	Molecular O <sub>2</sub>	60 °C	Alcohol (2 mmol), Catalyst (0.3 g), Toluene (5 ml)	100 (96) 100 (100) 100 (95) 100 (92)	The ruthenium hydroxalcite having Co cations was found to an efficient heterogeneous catalyst for the oxidation of alcohols in the presence of molecular oxygen. The catalyst was found to be highly reusable.	Kaneda et. al (1999)	20
Ruthenium/TEMPO	Molecular O <sub>2</sub>	100 °C	Alcohol(15mmol),Ru:TE MPO =1:3, PhCl (30 ml)	>99 (90) 97 (100) >99 (93)	The combination of RuCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub> and TEMPO affords an efficient catalytic system for the oxidation of benzyl alcohol, giving the corresponding aldehyde in >99% selectivity.	Sheldon et. al (2001)	21
Ru-Co-(OH) <sub>2</sub> -CeO <sub>2</sub>	Molecular O <sub>2</sub>	60 °C	Alcohol (2 mmol), Catalyst (0.3 g), benzotrifluoride (5 ml)	93(100)	The Ru-Co-(OH) <sub>2</sub> -CeO <sub>2</sub> acted as an excellent heterogeneous catalyst for aerobic oxidation of various types of alcohols.	Kaneda et. al (2002)	22
Ru-Co binary oxide	Molecular O <sub>2</sub>	110 °C	Alcohol (2.5 mmol), Catalyst (10; 1mol/mol with alcohol)), Toluene (10 ml)	54-100(76-95)	The Ru-Co oxide system was found to be active for the aerobic oxidation of alcohols.	Kozhenikov et. al (2003)	23
Pd/C	Air	80 °C	Alcohol, catalyst, solvent	86	The catalyst is fairly stable and yields are also good.	Chandalia et. al (1981)	24
Pd(OAc) <sub>2</sub> /pyridine/MS3A	Molecular O <sub>2</sub>	80 °C	Alcohol (1 mmol), base (0.1mmol), toluene (10ml)	96 97	The system of simple combination of commercially available reagents, Pd(OAc) <sub>2</sub> /pyridine/MS3A, has shown a high catalytic activity for aerobic oxidation of benzylic and aliphatic alcohols.	Uemura et. al (1998)	25
Pd(II)- supported hydroxalcite	Molecular O <sub>2</sub>	80 °C	Alcohol (1 mmol), pyridine (0.2-5mmol), toluene (5ml), catalyst (1.56mmol/g Pd)	74 94 98 100	The Pd(II)- supported hydroxalcite worked as an efficient catalyst for the oxidation of alcohols under oxygen.	Uemura et. al (2000)	26
Palladium(II) bathophenanthroline complex	Air	100 °C	Alcohol (10 mmol), NaOAc (1mmol), water, catalyst (0.05mmol)	100(99.8)	The Palladium (II) bathophenanthroline complex as a catalyst, water as a solvent, and air as the oxidant makes the reaction interesting from both an economic and environmental point of view.	Sheldon et. al (2000)	27
Pd(II)- supported hydroxalcite	Air	65-80 °C	Alcohol (1 mmol), pyridine (0.2mmol), toluene (10ml), catalyst (0.05mmol)	100 100 98	The Pd(II)- supported hydroxalcite worked as an efficient catalyst for the oxidation of alcohols under air at lower temperature.	Uemura et. al (2001)	28

**Table 1.1 (continued)**

I	II	III	IV	V	VI	VII	VIII
Pd-Ag (or monometallic Pd, Ag) supported on Pumice	Molecular O <sub>2</sub>	60 °C	Alcohol (0.05 ml), alcohol/Pd molar ratio = 100	-	For all the catalysts 100% selectivity was observed. Monometallic palladium catalyst showed the highest activity.	Liotta et. al (2001)	29
Pd(II)hydrotalcite	Molecular O <sub>2</sub>	80 °C	Alcohol (1.0 mmol), Pyridine (0.2 mmol), toluene (10 ml), Catalyst (0.05 mmol)	100 (100) 98 (91) 94 (87) 98 (94) 98 (92) 100 (97)	The catalyst is purely heterogeneous in nature, is shape selective, can be easily handled, easily prepared and reusable for several times.	Uemura et. al (2001)	30
Monodentate, nitrogen-based additives in combination with Pd(OAc) <sub>2</sub>	Molecular O <sub>2</sub>		Alcohol (1.2 mmol), Pd(OAc) <sub>2</sub> (0.036 mmol), THF (0.6 ml), Toluene (3.4 ml), Et <sub>3</sub> N (0.072 mmol), 3A MS (200 mg)	93 84	First report on the Pd-catalyzed aerobic oxidation of alcohol at room temperature. Earlier mechanistic studies revealed that the active catalyst might be a Pd-complex containing a single TEA ligand.	Sigman et. al (2002)	31
Pd-HAP-0 Pd-HAP-1	Molecular O <sub>2</sub>	90 °C	Alcohol (1mmol), trifluorotoluene (5 ml), Catalyst (0.1-0.3 g)	99 (100)	The PdHAP catalyst is suitable for large-scale reactions, is a recyclable with no leaching of Pd metal.	Kaneda et. al (2002)	32
Pd <sup>II</sup> -M oxides (M = Co, Cu, Fe and Mn)	Molecular O <sub>2</sub>	100 °C	Alcohol (2 mmol), Pd catalyst, toluene (10 ml)	53-95 (85-100%)	The reaction is purely heterogeneous in nature. It was suggested that the reaction takes place mostly by dehydrogenation mechanism.	Kozhenikov et. al (2003)	33
PS-PEG resin/palladium-phosphane	Molecular O <sub>2</sub>	Reflux	Alcohol (0.17 mmol), K <sub>2</sub> CO <sub>3</sub> (0.17 mmol), Catalyst (106 mg), water (0.9ml)	97	By using novel amphiphilic resin dispersion of palladium nanoparticles catalytic oxidation of alcohols was achieved in water, in high yields.	Uozumi et. al (2003)	34
Pd/Al <sub>2</sub> O <sub>3</sub>	Air	-	Benzyl alcohol (0.31M), Catalyst (100mg), mesitylene (0.14M), cyclohexane (30ml),	-	A complex reaction network has been observed during the liquid phase dehydrogenation and aerobic oxidation of Benzyl alcohol to Benzaldehyde.	Baiker et. al (2005)	35
CuCl <sub>2</sub> and Nitroxyl radical ion (or its hydroxy analogue)	Molecular O <sub>2</sub>	25 °C	Alcohol (10 mmol), nitroxyl ion (1 mmol), CuCl (1 mmol), DMF (25 ml)	96 97 92 91	This catalytic system provides an efficient method for the oxidation of alcohol to aldehyde as the sole product in high yields.	Semmelhack et. al (1984)	36

**Table 1.1(continued)**

I	II	III	IV	V	VI	VII	VI II
5% CuCl, 5% Phenanthroline, 5% DBADH <sub>2</sub>	Molecular O <sub>2</sub>	80-90 °C	Alcohol (0.4 mol), CuCl (20 mmol), 1,10-phenanthroline (20 mmol), Toluene (800 ml), K <sub>2</sub> CO <sub>3</sub> (0.80 mmol), DBAD <sub>2</sub> (20 mmol)	83 (100) 92 (95) 73 (87)	This process is not only economically viable and applicable to large-scale reactions, but it is also environmentally friendly.	Marko et. al (1996)	37
Polymer supported hypervalent Iodine (V) Resin	-	RT	Alcohol (1 equiv), DCM (15 ml), resin (1.75 equiv)	>95 (84) >95 (100) >95 (100) >95 (100)	First reported polymer supported periodinane resin reagent capable of converting a diverse collection of alcohols to corresponding aldehydes with sensitive structures.	Rademann et. al (2001)	38
Ni-Al-HT	Molecular O <sub>2</sub>	90 °C	Alcohol (2 mmol), Toluene (10 ml), Catalyst (0.5 g)	31-98	The process is not only economically viable but also applicable to large-scale reactions.	Choudhary et. al (2001)	39
TEMPO and polyoxometallate (H <sub>5</sub> PV <sub>2</sub> Mo <sub>10</sub> O <sub>40</sub> )	Molecular O <sub>2</sub>	100 °C	Alcohol (1 mmol), Polyoxomettalate (0.01mmol), TEMPO (0.03mmol), (0.15 ml in acetone)	99.6 (100) 98.3 (100) >99.9 (100) 98.7 (100)	It describes highly selective and active aerobic oxidation of alcohols in the presence of TEMPO as oxidant and polyoxometallate as co-oxidant.	Newmann et. al (2001)	40
Octahedral molecular sieves K-OMS-2 H-K-OMS-2	Air	110 °C	Alcohol (1 mmol), Toluene (10 ml), Catalyst (0.05 g)	90 (100) 97 (100) 95 (100) 99 (100)	First example of acid-catalyzed alcohol oxidation. Octahedral molecular sieves (K-OMS-2 and H-K-OMS-2) without use of additives gave high conversion/selectivity.	Suib et. al (2001)	41
Mn-Cu and Mn-Co-TEMPO	Molecular O <sub>2</sub>	-	Alcohol (12.5 mmol), TEMPO (1.25 mmol), Mn (NO <sub>3</sub> ) <sub>2</sub> (0.25mmol), Co (NO <sub>3</sub> ) <sub>2</sub> (0.25mmol), AcOH (12.5ml).	98 99 98 97 98	The combination of these catalyst Mn-Cu and Mn-Co-TEMPO could be a very effective for the aerobic oxidation of alcohols to aldehydes	Minisci et. al (2001)	42
Au/Fe <sub>2</sub> O <sub>3</sub>	Molecular O <sub>2</sub>	-	-	-	The presence of gold strongly enhances the catalytic activity of iron oxide, which is practically inactive under the same reaction conditions.	Galvagno et. al (2001)	43
N-hydroxyphthalimide	Molecular O <sub>2</sub>	RT	Alcohol (3 mmol), NHPI (0.3mmol), Co (OAC) <sub>2</sub> , mcpba(0.15 mmol), Acetonitrile	100(92) 85(94) 86(91)	This is a new selective synthesis of aromatic aldehydes by aerobic free-radical oxidation of benzyl alcohols by NHPI gives high yields.	Minisci et. al (2002)	44

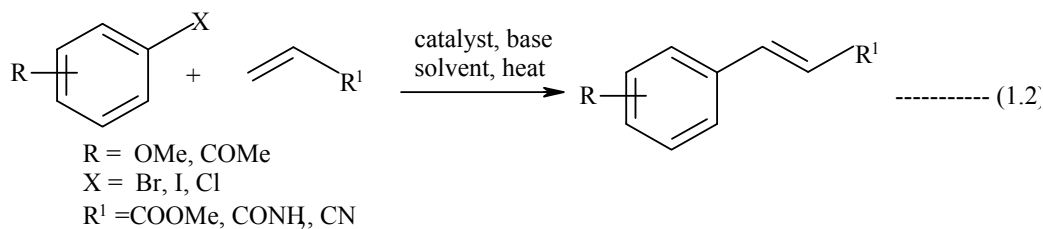


**Table 1.1** (continued)

I	II	III	IV	V	VI	VII	VIII
MnO <sub>4</sub> <sup>-</sup> -exchanged Mg-Al-hydrotalcite	TBHP	Reflux	Alcohol (52 mmol), TBHP (78 mmol) (70% TBHP in water), catalyst (0.5 g)	28.5 (84.4) 35.2 (99.8) 45.3 (98.4) 50.2 (99.7)	Higher the Mg/Al ratio, higher is the catalytic activity and basicity of the hydrotalcite catalyst. It also shows high activity for oxidation of benzaldehyde to benzoic acid.	Choudhary et. al (2003)	45
Non-noble transition metal containing hydrotalcite-like solid	Molecular O <sub>2</sub>	Reflux	Benzyl alcohol (96.6 mmol), Catalyst (0.5 g)	11.8 (97.3) 41.0 (70.8) 34.8 (83.7) 18.7 (99.5) 50.9 (70.1)	Among the transition metals (viz. Co, Ni, Cu, Zn, Fe, Mn and Cr) containing hydrotalcite-like solid materials, the Cu or Mn containing ones are promising catalysts for the solvent-free oxidation of benzyl alcohol.	Choudhary et. al (2003)	46
Transition metal containing LDH and/or mixed hydroxides	TBHP	94 °C	Alcohol (52 mmol), Catalyst (0.5 g), TBHP (68 mmol)	56.7 (77.4) 46.7 (91.3) 53.9 (70.6)	Out of all, the Mn, Cu and Co containing hydrotalcite like solid catalysts showed the best performance.	Choudhary et. al (2004)	47
Nano-size gold supported over different metal oxides	Molecular O <sub>2</sub>	130 °C	Benzyl alcohol (29 mmol), catalyst (0.1g), 5h	50 (95)	Among the supported gold catalysts (prepared by the HDP method), the Au/MgO, Au/Al <sub>2</sub> O <sub>3</sub> , Au/ZrO <sub>2</sub> , Au/La <sub>2</sub> O <sub>3</sub> and Au/U <sub>3</sub> O <sub>8</sub> catalysts showed high activity (benzyl alcohol conversion >50%) in the oxidation of benzyl alcohol by O <sub>2</sub> .	Choudhary et. al (2005)	48
Uranium oxide supported nano-gold	Molecular O <sub>2</sub>	130 °C	Benzyl alcohol (29 mmol), catalyst (0.1g), 5h	40.8 42.5 67 42.1	The catalyst is a highly promising with good selectivity and yields.	Choudhary et. al (2007)	49
9-Phenyl-10-methylacridium perchlorate	Molecular O <sub>2</sub>	Ambient	Benzyl alcohol, catalyst	-	The solvent-free selective oxidation of Benzyl alcohol to Benzaldehyde proceeds efficiently using AcPh <sup>+</sup> as an effective photocatalyst under visible light irradiation at ambient temperature.	Fukuzumu et. al (2006)	50
Artificial Enzyme [Ketocyclodextrins]	Aq. H <sub>2</sub> O <sub>2</sub>	RT	Alcohol (2ml), catalyst (1mg), 5h	-	These enzymes catalyze the oxidation of benzylic alcohols to aldehydes and the rate acceleration for the catalyzed reaction is very high.	Bols et. al (2006)	51

### 1.2.2 Heck Reaction

Heck olefination or simply the “Heck Reaction” (reaction 1.2) was discovered independently as early as the late sixties by R. F. Heck in [52] and initially received much attention as a new method for C-C bond formation. A few research groups continued to explore the scope and limitations of the method [53].



Heck reaction is an important tool for the C-C bond formation by the reaction between aryl halide and olefin. It is catalyzed by palladium in the presence of a base, and it has very important applications in synthetic organic chemistry to a variety of molecules.

Organic chlorides are the uncommon partners despite the fact that among the halides, chlorides are cheaper and easily available [54, 55]. The low reactivity of chlorides is usually due to the much larger strength of C-Cl bond (bond dissociation energies for Ph-Cl, Ph-Br and Ph-I are 96, 81, and 65 kcal/mol, respectively), which leads to reluctance by aryl chlorides to oxidatively add to Pd (0) centers, a critical step in the palladium-catalyzed coupling reactions and hence, developing new catalyst systems for aryl chloride activation is a challenging task.

Many homogeneous catalyst systems are known for the Heck reaction [56]. In 1990's, heterogeneous Heck reaction was extensively studied due to its popularity and its applicability in the industry. Heterogeneous catalysts comprising clay-supported Pd-Ph<sub>2</sub>-P-Si has been employed for the coupling reaction [57]. A Palladium-copper-exchanged montmorillonite K-10 clay catalyst has been described, which can catalyse the preparation of stilbene from aryl

halides and styrenes with high yields [58]. Important advantages of Heck reaction are the broad availability of aryl halides and tolerance of the reaction for a wide variety of functional groups. Ying and co-workers [59], Djakovitch and co-workers [60], Arai and co-workers [61, 62] and Iyer and co-workers [63] were studied the action of heterogeneous catalysts thoroughly.

Use of a number of other heterogeneous catalysts, such as silica-supported palladium [64], palladium on carbon [65], palladium supported on various metal oxides and zeolites [66], palladium supported hydrotalcite [67], MCM-41 supported aminopropylsiloxane palladium complex [68], Pd-complexes of silica-anchored nitrogen containing chelating compounds [69], Pd-zeolite catalysts [70], palladium and non-cross-linked amphiphilic polymer [71], Pd-SAPO-31 [72] for aryl chlorides, basic zeolites containing palladium as bifunctional catalysts [73], Pd on activated carbon [74], alkali-exchanged sepiolites-containing palladium as bifunctional catalysts [75], dicyano-functionalized MCM-41 anchored-palladium complexes [76], Pd-iminopyridyl complexes supported on chitosan [77], has been reported for the Heck reaction.

Some other examples of heterogeneous catalysts are palladium supported on single wall carbon nanotubes [78], the combination of palladium acetate and DABCO<sub>3</sub> [79], Pd deposited on organic-inorganic hybrid supports [80], Nafion-Teflon bimembrane supported palladium catalyst [81], palladium collide layer grafted mesoporous SBA-15 material [82], layered double hydroxide supported nanoplatinum catalyst [83], and polymer supported N-heterocyclic carbene-palladium complex [84].

The fact that no inert atmosphere and no ligands are necessary, the ease of catalyst separation and the potential to increase the existing catalyst activity makes supported Pd catalysts an important alternative to homogeneous catalysts for industrial applications of the

Heck reaction. A detailed literature survey for the Heck reaction using different catalysts is presented in Table 1.2.

**Table 1.2** Summary of work on the Heck Reaction

Catalyst	Reaction condition		Conversion (%) (Selectivity %)	Remarks, if any	Investigator (Year)	Ref
	Temp.	Reaction mixture				
I	II	III	IV	V	VI	VII
(Montmorilloniteethylsilyldiphenyl phosphine)PdCl <sub>2</sub> Clay anchored catalyst	100 °C	Aryl halide (22mmol), olefin (20mmol), tributylamine (25mmol), catalyst (50mg)	99(98)	Clay anchored catalysts is a better route for high activity and selectivity	Choudary et. al (1992)	57
Pd-Cu-Mont.K10	Reflux	Arylhalide(3mmol), Acrylate(6mmol),K <sub>2</sub> CO <sub>3</sub> (8mmol),catalyst (10% wrt.aryl halide), DMF (5ml)	93(100)	The high activity is attributed to a synergistic effect produced by the presence of Pd and Cu species in the catalysts	Sudalai et. al (1997)	58
Pd-Grafted-mesoporous MCM-41 [Pd-TMS11]	120-170 °C	Arylhalide(49mmol), Olefin(60mmol), Triethylamine(52.4mmol),Dodecane(31.7),DMA(48 ml), 0.02mol%catalyst, 20min-48hrs,GC	100(99)	The Catalysts system Pd-TMS11 is prepared by vapor grafting. and gives excellent activity.	Ying et. al (1997)	59
Pd-Modified zeolites	140 °C	Arylhalide(10mmol), Olefin(15mmol),NaOAc(15mmol),catalyst(0.2mol%),DMAc(8ml),	51-95	Remarkably the small amounts of Pd (0.2mol %) exhibit a high activity towards the Heck reaction.	Djakovitch et. al (1999)	60
Pd/TPPTS-KOAC	80-130 °C	Arylhalide(10mmol), Olefin(20mmol),KOAc(10mmol), catalyst(0.1mmol)Toluene	90(100)	The supported ethylene glycol phase Pd/TPPTS catalyst with inorganic base is highly effective system.	Arai et. al (1999)	61

**Table 1.2 (continued)**

I	II	III	IV	V	VI	VII
Pd/C	110 °C	Arylhalide(5mmol), Olefin(5mmol), Na <sub>2</sub> CO <sub>3</sub> (2.5mmol), catalyst(40 mg), TEA (1 mmol), NMP/H <sub>2</sub> O (30 ml)	100(70)	The use of both TEA and Na <sub>2</sub> CO <sub>3</sub> is effective in promoting the Pd redeposition as well as the rate of reaction.	Arai et. al (2000)	62
Ni, Co, Cu and Mn heterogeneous catalysts	150 °C	Arylhalide(1mmol), Olefin(5mmol), NMP(5ml), (2mmol)K <sub>2</sub> CO <sub>3</sub> , Catalyst (0.025g)	23-95	The products were obtained in good yields	Iyer et. al. (2000)	63
Silica supported palladium Catalysts	82 °C	Arylhalide(30mmol), Olefin(30mmol), Et <sub>3</sub> N(30mmol), Acetonitrile (30ml), Catalyst(0.25g), Dodecane(Internal Standard)	15-82	The catalyst is prepared through sequential grafting of organic functional groups and through preconditioning which shows good activity.	Clark et. al (2000)	64
Pd/C in ionic liquid	100 °C	Arylhalide(1mmol), Olefin(1.5mmol), Et <sub>3</sub> N(1.5mmol), Catalyst(0.031mmol), [bmim]PF <sub>6</sub> (1ml)	86	The major advantage of the present protocol is that the catalyst system is easily re-usable without loss of catalytic activity.	Hagiwara et. al (2001)	65
Pd supported on metal oxides and zeolites	140 °C	Arylhalide(10mmol), Olefin(15mmol), NaOAc(15mmol), DMAc (10ml), Catalyst (0.1mol%)	90(100)	The Pd supported on metal oxides and zeolites exhibits high activity and selectivity in this arylation reaction	Djakovitch et. al (2001)	66
Pd containing hydrotalcite	140 °C	Arylhalide (3mmol), Olefin (3.9mmol), Triethylamine (3.6mmol), dry DMF, Catalyst	59-88	Pd-hydrotalcite is a active catalyst for this reaction.	Sivasanker et. al (2002)	67
MCM-41 supported aminopropylsiloxane pd(0) complex	70 °C	Arylhalide(10mmol), Olefin(15mmol), Et <sub>3</sub> N (35mmol), DMF (6ml), N <sub>2</sub> Catalyst(0.0312mmol), 2h.	84-98	This complex has high activity and stereoselectivity for Heck reaction.	Zhou et. al (2002)	68

**Table 1.2 (continued)**

I	II	III	IV	V	VI	VII
Pd complexes anchored on silica with chelating nitrogen ligands	Reflux	Arylhalide(51.6mmol),Olefin(60.5mmol), Bu <sub>3</sub> N (54.3mmol), Toluene (20ml), Catalyst(0.2g),2h	89(97)	The use of stable anchored Pd complexes can offer an interesting alternative to homogeneous catalysts for industrial applications.	Moggi et. al (2002)	69
Pd-Zeolites	130 °C	Arylhalide (3mmol), Olefin (4.5mmol), NaOAC (3.3mmol), DMA/Toluene (3ml), Catalyst (0.125mol%), 20h	75	These catalysts are not only active and selective but also truly heterogeneous catalysts.	Jacobs et. al (2002)	70
PdAS-V (Palladium and non-cross-linked amphiphilic polymer)	100 °C	Arylhalide (36.5mmol), Olefin (54.7mmol), Et <sub>3</sub> N (54.7mmol), Toluene (18ml), Catalyst (5 mg)	90-98	The heterogeneous Heck reaction using PdAS-V afforded the corresponding coupling products in high yields.	Ikegami et. al (2003)	71
Pd-SAPO-31 Catalyst	60-120 °C	Arylhalide(1mmol),Olefin(2mmol), Et <sub>3</sub> N (1.5mmol), DMF (5ml), Catalyst(4wt%),2h	99.8(97.9) 100(98.8) 100(96.8) 98.9(97.2) 98.3(96.8) 99.4(78.1)	This catalysts also shows a very good activity for aryl chlorides	Ratnasamy et. al (2003)	72
Basic Zeolites containing Pd as bifunctional catalysts	153 °C	Arylhalide(2.8mmol),Olefin(5.6mmol), K <sub>2</sub> CO <sub>3</sub> (7.22mmol), DMF (5ml), Catalyst(100mg),3h	40-100	This bifunctional PdCl <sub>2</sub> -CsX catalyst is active for several other substrates	Corma et. al (2004)	73
Pd on activated carbon	140 °C	Arylhalide (10mmol), Olefin (15mmol), NaOAC (12mmol), NMP (8ml), Catalyst (0.1mol%), 4h	92	The fundamental applicability of simple heterogeneous Pd/C catalysts for one-pot synthesis has been demonstrated by organic syntheses of several important substructures of natural and pharmaceutical compounds and therefore this one-pot synthesis is preferable and can be performed as tandem and consecutive reaction.	Koehlar et. al (2004)	74

**Table 1.2** (continued)

I	III	IV	V	VI	VII	VIII
Alkali exchanged sepiolites containing palladium as bifunctional catalysts	145 °C	Arylhalide (0.15mmol), Olefin (0.18mmol), O-Xylene (5 ml), Catalyst (1 g), 24h.	24-87	The palladium containing basic sodium sepiolites that can be used as a bifunctional catalysts for the Heck reaction using O-xylene as solvent, the process is truly heterogeneous.	Garcia et. al (2004)	75
Dicyano-functionalized MCM-41 anchored palladium complexes	70 °C	Arylhalide, Olefin, Et <sub>3</sub> N (10 ml), anhydrous DMF (20 ml), Catalyst.	-	The dicyano-functionalized MCM-41 anchored Pd complexes as the Heck reaction heterogeneous catalysts showed easy recovery, high activity and reusability.	Zhang et. al (2004)	76
Pd-iminopyridyl complexes supported on chitosan	25 °C	Arylhalide (5.3mmol), Olefin (5.3mmol), Et <sub>3</sub> N (10mmol), Catalyst(25mg), anhydrous dioxane(30ml)	82 88	Chitosan is an interesting support for catalysis due to its stability, and lower acidity.	Macquarrie et. al (2004)	77
Pd supported on single wall Carbon nanotubes (SWNT)	140 °C	Arylhalide (4.44mmol), Olefin (6.69mmol), Bu <sub>3</sub> N (8.92 mmol), DMF (5ml), Catalyst (3mg)	-	The known ability of SWNT to adsorb gases in even higher quantities than activated carbons, and this co-operates the success of the reaction.	Corma et. al (2005)	78
Pd (OAc) <sub>2</sub> /DABCO	120 °C	Arylhalide (0.5mmol), Olefin (0.75mmol), DMF (3ml), Catalyst (1:2), K <sub>2</sub> CO <sub>3</sub> (1eq.)	50-100	This is an efficient catalytic system for the reaction and gives excellent yields.	Li et. al (2005)	79
Pd deposited onto organic-inorganic hybrid silica materials	150 °C	Arylhalide (0.89mmol), Olefin (0.89mmol), NaOAc (0.89mmol), NMP(1.5ml), Catalyst (68 mg)	94(85) 97(100) 87(21) 75(31)	The palladium on silica catalysts thus prepared were found to exhibit high activity and selectivity in the Heck coupling with aromatic iodo and activated bromo compounds.	Molnar et. al (2005)	80
Nafion-Teflon bimembrane-supported palladium Catalyst	100 °C	Arylhalide (1.5eq.), Olefin (1.5eq.), Et <sub>3</sub> N (2eq.), CH <sub>3</sub> CN, Catalyst (0.8mol %)	80-98	A diphenyl-phosphino ligand attached to the surface of a Nafion-Teflon bimembrane and demonstrated its utility in the Heck reaction and it has exceptional stability of the ligand and the recyclability of the catalyst.	Wang et. al (2005)	81

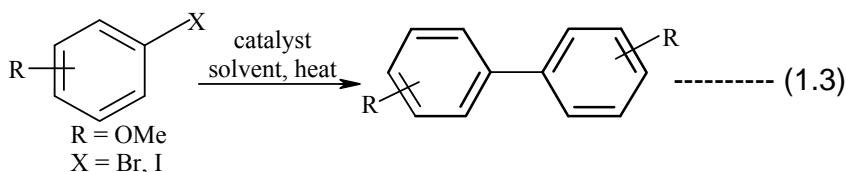


**Table 1.2 (continued)**

<b>I</b>	<b>III</b>	<b>IV</b>	<b>V</b>	<b>VI</b>	<b>VII</b>	<b>VIII</b>
Palladium collide layer grafted mesoporous SBA-15 material [Pd – SBA]	120 °C - 170 °C	Arylhalide (20mmol), Olefin (30mmol) (22mmol), Et <sub>3</sub> N (22mmol), dodecane (10mmol), NMP (20ml), Catalyst (0.02mol%), 2-48h	100(88) 37(85) 99(97) 95(99) 100(91) 50(94) 100(98) 100(99)	Mesoporous SBA-15 catalyst was used as the support since its well-defined, large pore opening provided easy access for large substrate molecules.	Shi et. al (2005)	82
Layered Double Hydroxide-supported nanoplatinum	135 °C	Arylhalide (0.5mmol), Olefin (0.75mmol), NaOAc (1.5mmol), NMP (3ml), Catalyst (1 mol %)	67-94	This LDH-Pt <sup>0</sup> catalyst is an efficient, simple protocol and can be easily recovered for Heck reaction.	Choudary et. al (2006)	83
Polymer-supported N-heterocyclic carbene-Pd complex	120 °C	Arylhalide (1mmol), Olefin (1.3eq.), TBA (1.5eq.) DMA (10ml), Catalyst (1mol%), 3h	70-95	The use of a stable and reusable polymer supported N-heterocyclic carbene-Pd complex for the Heck reaction with high yield in a shortened reaction time, due to the high efficiency of the NHC-Pd complex located solely on the surface of the polymer supported resin.	Lee et. al (2006)	84

### 1.2.3 Ullmann Reaction

The Ullmann reaction, initially reported in 1901 [85], has long been employed by chemists to generate a C-C bond between two aromatic nuclei. Typically, the Ullmann reaction (reaction 1.3) is an important tool for generating the C-C bond formation between aryl halide (two molecular equivalent) in the presence of one equivalent of finely divided copper at high temperature (above 170 °C) to form a carbon-carbon bond with elimination of copper halide for the preparation of symmetrical, unsymmetrical biaryls and biphenylenes.



Copper is particularly very effective in this type of condensation. This procedure and variants were comprehensively reviewed several decades ago [86-88]. The traditional version of the Ullmann reaction requires harsh reaction conditions, and the reaction has a reputation for erratic yields. Since its discovery, some improvements and alternative procedures have been introduced. Considerable improvements have been made through the last century. Dimethylformamide is a solvent, which permits the use of lower temperature and a lower proportion of copper. Besides this the use of an activated form of copper powder, made by the reduction of copper (I) iodide with potassium, allows the reaction to be carried out at even lower temperature (about 85 °C) with improved yields. As the reaction is heterogeneous, it can be accelerated considerably using ultrasound [89].

The major limitation of the original Ullmann reaction was the obtaining of only symmetrical biaryls. Several attempts to synthesize unsymmetrical biaryls have been made and some success has been achieved by associating aryl halides of different reactivities. These

extensions of the original Ullmann reaction to unsymmetrical biaryls formation did however require the use of a significant excess of the “activated” aryl.

Then recently there is a review on uses of stoichiometric amounts of copper, nickel, zinc and palladium as a reagent/catalyst [90], where biaryl axis is the central building block in a very large number of natural products of differing structure, biological activity and biosynthetic origin, including for example polyketides, terpenes, lignans, coumarins, flavonoids, tannins, peptides and alkaloids.

Some other examples of the Ullmann coupling are with zero valent nickel promoted coupling [91] to form biaryls and first synthesis of Alnusone, novel palladium catalyzed couplings in presence of equimolar amounts of trialkylamine as a co-catalyst [92], homocoupling of aryl halide by palladium acetate and tetra-*n*-butylammonium bromide mixture [93] for the preparation of functionalized biphenyls.

There is a report on carbon-carbon bond formation via palladium catalyzed zinc mediated aryl halide coupling in air and aqueous acetone at an ambient temperature [94], where catalytic palladium is used for the inter and intramolecular homocoupling of aryl halides in the presence of hydroquinone [95]. Recently Li et.al have reported the catalytic amount of 18-crown-6 and zinc mediated reductive coupling of aryl halides catalyzed by palladium on carbon [96] at ambient temperature in water under air atmosphere.

Then recently there is a report on first low valent metal catalyzed coupling of aryl halides using  $[(PPh_3)_nNi(O)]$  as catalyst [97] and [bmim]PF<sub>6</sub> as a solvent, nickel catalyzed coupling with aromatic Grignard reagent [98] at ambient temperature in high yield, kinetics and process parameters of coupling of chloroaryls in the presence of zinc, water and catalytic palladium on carbon [99] have been studied.

There is a report on palladium catalyzed Ullmann-type coupling with zinc in presence of water and liquid carbon dioxide [100], fluorinated palladium catalyzed coupling reaction in supercritical carbon dioxide [101] under solventless conditions, synthesis of symmetrical functionalized biaryls from aryl halides catalyzed by commercial zinc dust using ammonium formate [102] in comparatively high yield have been reported.

One pot synthesis of symmetrical biaryls [103] was reported where biaryls play an important role in modern organic chemistry like natural products having biological activity contain symmetrical or unsymmetrical biaryl units such as Michellamine A or the secalonic acid. There was a report on convenient TDAE/palladium promoted homocoupling reaction using the ionic liquid [bmim]PF<sub>6</sub> as a solvent [104], L-Proline promoted Ullmann-type coupling with CuI and imidazole [105] with excellent yield, sonochemical zinc mediated Ullmann homocouplings were carried out in an aqueous media under CO<sub>2</sub> bubbling in presence of Pd/C [106] made biaryl synthesis both more efficient and greener.

To substantiate the fact that, the easy catalyst separation, recycling and the potential to increase the existing catalyst activity, make supported Pd catalysts an important alternative to homogeneous catalysts for industrial applications. A detailed literature survey of these studies is presented in Table 1.3.

**Table 1.3** Summary of Work on the Ullmann Reaction

Catalyst	Reaction condition		Conversion (%) (Selectivity %)	Remarks, if any	Investigator (Year)	Ref
	Temp	Reaction mixture				
I	II	III	IV	V	VI	VII
Zero valent Nickel complex [Ni(COD) <sub>2</sub> ]	50 °C	Arylhalide (1.8 mol/mol of catalyst), Catalyst (0.5mol equi.), DMF (5ml), 20h.	82 71 83	The coupling of aryl and with zerovalent nickel complexes gave comparable yields under mild conditions.	Semmelhack et. al (1981)	91
Pd catalysed triphenylarsine as co-catalyst	140 °C	Arylhalide (100mmol), NBu <sub>3</sub> (110mmol), Pd(OAC) <sub>2</sub> (0.5mmol), Triphenylarsine (1 mmol), DMF, 24h	50	The new biaryl synthesis was discovered by novel Pd-catalysed with haloarenes	Heitz et. al (1991)	92
Pd(OAC) <sub>2</sub> and nBu <sub>4</sub> NBr as Catalyst	115 °C	Arylhalide (1equiv), Catalyst (0.05/0.5), DMF/H <sub>2</sub> O (0.9ml/0.35ml), K <sub>2</sub> CO <sub>3</sub> (1 equiv.)	81	The association of Pd (OAC) <sub>2</sub> and nBu <sub>4</sub> NBr is a powerful and convenient catalyst for the Ullmann reaction and used for the preparation of functionalized biphenyls directly from the corresponding halide with catalytic amounts of a metal derivative.	Lemaire et. al (1998)	93
Pd/C+Zinc powder+ air atmosphere	RT	Arylhalide (100mg), Catalyst (80mg), Zinc powder (80mg), water/acetone (4ml), air atmos	92 94	This air stable palladium catalytic system provides an operational convenience for synthesis.	Li et. al (1999)	94
Pd (OAC) <sub>2</sub> and As (o-tolyl) <sub>3</sub> +hydroquinone	75 °C	Arylhalide, Pd(OAC) <sub>2</sub> (2mol%), hydroquinone(50mol%), CS <sub>2</sub> CO <sub>3</sub> (100mol%)	95	The procedure is relatively mild and appears to have broad applicability and also use of hydroquinone as a stoichiometric in situ reductant of higher oxidized palladium species.	Rawal et. al (1999)	95
Pd/C-Zn +18-crown-6	RT	Arylhalide(300mg), Catalyst(291mg), 18-crown-6(73mg), Zinc powder(273mg), Water(10ml)	51 54	The use of catalytic amount of 18-crown-6, the zinc mediated reductive coupling of aryl halides catalyzed by Pd/C at ambient temperature, in water and air allows them to obtained good yields.	Li et. al (2000)	96
[(PPh <sub>3</sub> ) <sub>n</sub> Ni(0)] + Ionic liquid [bmim]PF <sub>6</sub>	80 °C	Arylhalide (10mmol), catalyst (5mmol), PPh <sub>3</sub> (10mmol), Zn powder(10mmol), [bmim]PF <sub>6</sub> (25ml), 48h	87 55	The yields of biaryls were found to be satisfactory.	Howarth et. al (2000)	97

**Table 1.3** continued

I	III	IV	V	VII	VII	VIII
Nickel catalyst with aromatic Grignard reagent	RT	Arylhalide (1eq.), Grignard reagent (1.5eq.), Ni(OAC) <sub>2</sub> (3mol%), Ligand(3mol%), THF(3ml)	-	The highly active catalysts based on nickel as the catalytically active metal were developed for the Grignard coupling reaction of aryl chlorides at ambient temperature and at low catalyst loading.	Herrmann et. al (2000)	98
Pd/C – Zinc+water	100 °C	Arylhalide (45mmol), Catalyst (5%), NaOH (125mmol), PEG-400 (8.4mol% of substrate), water (50ml), Zinc (50mmol)	-	The zinc mediated coupling in presence of water and Pd/C seems to be good combination for the formation of biaryls	Sasson et. al (2000)	99
Pd/C +Zinc	RT	Arylhalide (2mmol), catalyst (400mg), Zn (260mg), Water (1ml), CO <sub>2</sub> (6Mpa)	54 58	The use of carbon dioxide as an environmentally benign solvent has been one of the success stories of green chemistry.	Li et. al (2002)	100
Pd(OCOCF <sub>3</sub> ) <sub>2</sub> /P(2-furyl) <sub>3</sub> in scCO <sub>2</sub>	80 °C	Arylhalide (1.78mmol), catalyst (11.9mg), Tris-2-furylphosphine (16.6mg), DIPEA (2.87mmol), CO <sub>2</sub> (11Mpa), 15h	95	The choice of solvent played a critical role in the development of a clean process.	Rayner et. al (2002)	101
Zinc/ammonium formate	Reflux	Arylhalide (5mmol), MeOH(15ml), zinc dust(5mmol), ammonium formate(10mmol), NaOH(5mmol)	96 94	The Zinc/ammonium formate system, the coupling of aryl halides proceeds efficiently to give biaryls in high yields.	Gowda et. al (2004)	102
PdCl <sub>2</sub> dppf	80 °C	Arylhalide (1equi.), PdCl <sub>2</sub> dppf (4mol %), K <sub>2</sub> CO <sub>3</sub> (3equi.), reagent (0.5equi.), DMSO(6ml)	98 77	The procedure developed here is an easy and widely applicable for the synthesis of symmetrical biaryls and gives high yields of biaryls.	Brase et. al (2004)	103
TDAE/Pd in [bmim]PF <sub>6</sub>	120 °C	Arylhalide (1mmol), catalyst (5mol%), TDAE (2equi.), Ionic liq. (2ml), 2h, GC	98 88	They have developed an efficient and recyclable TDAE/Pd promoted reaction using an Ionic liquid.	Alper et. al (2004)	104

**Table 1.3** continued

<b>I</b>	<b>III</b>	<b>IV</b>	<b>V</b>	<b>VII</b>	<b>VII</b>	<b>VIII</b>
L-proline ligand/CuI/IL	110 °C	Arylhalide (2mmol.), Imidazole(2.2mmol), CuI(0.2mmol), L-proline(0.4mmol), K <sub>2</sub> CO <sub>3</sub> (5mmol), [Bmim]BF <sub>4</sub> (4ml)	-	This system L-proline ligand/CuI/IL is a mild and efficient method for the copper catalysed coupling of imidazoles with vinyl halides and ionic liquid works an excellent media for the coupling reaction.	Bao et. al (2005)	105
Pd/C –Zinc mediated under Ultrasound	45 °C	Arylhalide (1mmol.), catalyst, Zinc dust, DME/Water (1:1)	58	The sonochemical zinc mediated Ullmann homocouplings were successfully carried out in aqueous media under CO <sub>2</sub> bubbling in the presence of Pd/C and are efficient and greener process.	Cravotto et. al (2005)	106

### 1.3 OBJECTIVES AND SCOPE

This Ph.D. work was undertaken as a part of the comprehensive research programme in our laboratory for replacing homogeneous catalysts by novel reusable heterogeneous solid catalysts for the synthesis of fine chemicals, with the following objectives.

1. To study oxidation of benzyl alcohol by tert-butyl hydroperoxide (TBHP) to benzaldehyde using novel reusable solid catalysts, such as
  - Anion  $\text{MnO}_4^-$ -exchanged Mg-Al-hydrotalcite
  - Layered double hydroxides (LDHs) containing one or two different transition elements. (Viz. Ni, Co, Zn, Cu, Fe, Mn and Cr)
  - Nano-gold supported on alkaline earth oxides,
  - Nano-gold supported on Gr.IIIa oxides,
  - Nano-gold supported on transition metal oxides
  - Nano-gold supported on rare earth oxides.
2. To study a) effect of catalyst preparation method and b) the influence of the reaction parameters (viz. base, solvent, temperature and time) on the arylation of styrene with aryl halide, using a novel reusable solid catalyst ( $\text{Pd/ZrO}_2$ ) in the Heck coupling reaction.
3. To study the influence of base, solvent, temperature and time on the Ullmann coupling reaction, using a novel reusable solid catalyst ( $\text{Pd/ZrO}_2$ ) for biaryl formation.



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## **CHAPTER-2**

### **EXPERIMENTAL**



## CHAPTER-2

### EXPERIMENTAL

#### 2.1 GASES AND CHEMICALS

The following gases and chemicals have been used.

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Hydrogen	– IOLAR-II Grade, Indian Oxygen Ltd., Mumbai.
Nitrogen	– IOLAR-II Grade, Indian Oxygen Ltd., Mumbai.
Air	– IOLAR-II Grade, Indian Oxygen Ltd., Mumbai.
Aluminium nitrate	98.5 % Loba Chem., Mumbai.
Magnesium nitrate	99 % S. D. Fine Chemicals, Mumbai.
Ferric nitrate	98 % Qualigens, Mumbai, India.
Gallium oxide	99.99 % Aldrich, USA.
Indium nitrate	99.99 % Aldrich, USA.
Thallium nitrate	99.99 % Aldrich, USA.
Calcium oxide	Loba Chem., Mumbai.
Barium oxide	Loba Chem., Mumbai.
Strontium oxide	99 % S. D. Fine Chemicals, Mumbai.
Magnesium oxide	Loba Chem., Mumbai.
Sodium carbonate	Qualigens, Mumbai.
Silica	Fuji Davison $\beta$ -type (white)
Ferric nitrate	98%, Qualigens, Mumbai.
Cobalt oxide	Loba Chem., Mumbai.
Nickel oxide	SD Fine chem., Mumbai.
Copper oxide	Robert Johnson
Lanthanum oxide	99.99 % Aldrich, USA.
Cerium nitrate	99.9 % Loba Chem., Mumbai.
Gadolinium oxide	99.99 % Aldrich, USA.
Samarium oxide	Loba Chem., Mumbai.
Antimony oxide	Loba Chem., Mumbai.
Europium oxide	99.99 % Aldrich, USA.

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Terbium oxide	99.99 % Aldrich, USA.
Erbium oxide	99.99 % Aldrich, USA.
Ytterbium oxide	99.99 % Aldrich, USA.
Uranyl nitrate	BDH, Mumbai.
Hydrochloric acid	35 % Merck, Mumbai.
Nitric acid	69 –72 % Thomas Baker, Mumbai,
Sulphuric acid	98 % Merck, Mumbai.
Urea	99.5 % Loba Chem., Mumbai.
<i>tert</i> -butyl hydroperoxide	70 % aqueous Lancaster, UK.
Benzaldehyde	98.5 % S. D. Fine Chemicals, Mumbai.
Benzoic acid	99.0 % Renal, Hungary.
Toluene	(AR Grade) S. D Fine, Chemicals, Mumbai.
<i>p</i> -Xylene	(>99%) Fluka, Switzerland.
Anisole	(EP Grade) S. D Fine, Chemicals, Mumbai.
Silica gel (60-120 mesh)	Sisco Research Laboratory Pvt. Ltd., Mumbai.
Phenolphthalein	Merck (India) Pvt. Ltd., Mumbai.
1,4-dioxan	Merck (India) Pvt. Ltd., Mumbai.
NMP	99.99% SD Fine Chem., Mumbai.
Pyridine	Sisco Research Laboratory Pvt. Ltd., Mumbai.
Gold chloride	99.9% Thomas Baker.
Benzyl alcohol	99.99% SD Fine Chem., Mumbai.
Neodymium acetate	Lancaster, UK.
Ethyl acetate	LR, S. D. Fine
Pet ether	LR, S. D. Fine
Dichloromethane	LR, S. D. Fine
Chloroform	LR, S. D. Fine
CDCl <sub>3</sub>	Aldrich
Carbon tetrachloride	LR, S. D. Fine

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Palladium chloride	Lancaster Chemicals 99.0%
Zirconyl nitrate	Loba-Chemical Ltd. 99.0%
Bromobenzene	Lancaster Chemical 99.0%
Chlorobenzene	E-Merck 99.5%
Styrene	99.0%, Lancaster Chemicals
Stilbene	Aldrich 96.9%
N, N Dimethylformamide	E-Merck 99.5%
Potassium carbonate	Ranbaxy 99.0%
Potassium hydroxide	S. D Fine Chemicals, Mumbai.
Potassium carbonate	S. D Fine Chemicals, Mumbai.
Iodobenzene	Lancaster chemical 99.0%
Iodoanisole	Aldrich 99.0%
Acryl amide	S. D Fine Chemicals, Mumbai.
Acrylonitrile	S. D Fine Chemicals, Mumbai.
Ethyl acrylate	Lancaster Chemicals 99.0%
Methyl acrylate	Lancaster Chemicals 99.0%
4-Bromo acetophenone	Lancaster Chemicals 99.0%
3-Bromo acetophenone	Lancaster Chemicals 99.0%
Anisaldehyde	S. D Fine Chemicals, Mumbai.
3,4,5-trimethoxy benzaldehyde	Lancaster Chemicals 99.0%
3,5-dimethoxy benzaldehyde	Lancaster Chemicals 99.0%
3,4 -dimethyl benzaldehyde	Lancaster Chemicals 99.0%
Sodium carbonate	S. D Fine Chemicals, Mumbai.
Zinc dust	S. D Fine Chemicals, Mumbai.
Sodium acetate	99.99% SD Fine Chem., Mumbai.
Triethyl amine	Aldrich 99.0%

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## **2.2 CATALYST PREPARATION**

### **2.2.1 Preparation of Mg-Al-hydrotalcite and other Hydrotalcite-like Catalysts**

The Mg-Al-hydrotalcite catalysts with Mg/Al ratio of 2, 3, 5 and 10 were prepared as follows. Mg-Al-hydrotalcite was synthesized by adding two aqueous solutions, one containing magnesium nitrate and aluminium nitrate with required Mg/Al ratio and second containing potassium hydroxide and potassium carbonate, into a flask containing deionized water under vigorous stirring at 40 °C, while maintaining a constant pH of 11-12, similar to that described earlier [1]. The resulting white gel was aged for 0.5 h and then filtered, thoroughly washed and then dried at 80 °C in vacuum oven for 12 h. The resulting Mg-Al-hydrotalcite was powdered. Similarly other hydrotalcite-like catalysts were prepared by same procedure as given above like Mn-Al, Co-Al, Ni-Al, Zn-Al, Mg-Fe, Mn-Fe, Co-Fe, Ni-Fe, Mn-Cr, Co-Cr, Ni-Cr, Cu-Cr, and Zn-Cr hydrotalcite.

### **2.2.2 MnO<sub>4</sub><sup>-1</sup>-exchanged Mg-Al-hydrotalcite Catalysts**

The Mg-Al-hydrotalcite was calcined at 600 °C for 4 h. The Mg-Al-hydrotalcite (13 g) was treated under stirring with an aqueous solution of KMnO<sub>4</sub> (1.58 g in 100 ml water) at 80 °C for 24 h. The resulting MnO<sub>4</sub><sup>-1</sup>-exchanged Mg-Al-hydrotalcite was filtered and washed with hot deionized water and then dried at 80 °C in vacuum oven. The amount of MnO<sub>4</sub><sup>-1</sup>-exchanged was determined with the help of amount of KMnO<sub>4</sub> present in the filtrate and washing. Before using, the MnO<sub>4</sub><sup>-1</sup>-exchanged Mg-Al-hydrotalcite catalysts were heated in an air oven at 200 °C for 2 h.

### 2.2.3 Preparation of Supported Gold Catalysts

The supported gold catalysts were prepared by four different methods as follows:

#### 2.2.3.1 Impregnation Technique

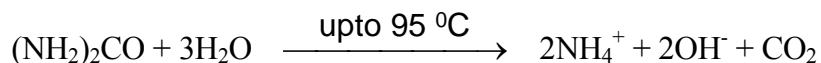
In this method, the catalyst was prepared by the incipient wetness technique by contacting the metal oxide support (2.0 g) with an aqueous solution of  $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$  containing the required amount of gold, evaporating the water on water bath with vigorous stirring and drying at  $100\text{ }^\circ\text{C}$  for 12 hours and finally calcining the solid in air at  $400\text{ }^\circ\text{C}$  for 2 h.

#### 2.2.3.2 Deposition-Precipitation Method (DP)

In a typical deposition-precipitation procedure, a known amount of an aqueous solution of  $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$  was added to distilled water and heated under constant stirring at a temperature of  $70\text{ }^\circ\text{C}$ . The pH of the solution was adjusted (except when alkaline earth oxides were used) using sodium hydroxide (NaOH) to about 7.0. The metal oxide support was then added to the stirred solution and the pH was again adjusted to 7.0. The slurry was aged for 1.0 h, the solid particles were washed with 4 liters of deionized water (500 ml x 8 times) to remove chlorides and free  $\text{Au}(\text{OH})_3$  and then filtered. The resulting material was then dried at  $90\text{ }^\circ\text{C}$  for overnight and calcined in air at  $400\text{ }^\circ\text{C}$  for 2 h.

#### 2.2.3.3 Homogeneous Deposition Precipitation Method (HDP)

In this method, an aqueous solution of urea  $(\text{NH}_2)_2\text{CO}$  is utilized to generate ammonium hydroxide as a precipitating agent at elevated temperature, according to the reaction.



Thus urea can be used as a precursor for the hydrolyzing agent. In a typical procedure, a known amount of an aqueous gold chloride ( $\text{HAuCl}_4$ ) solution was added to 300 ml of distilled water. A known quantity of urea (generally 50 times more than that required for precipitating the gold from the solution) was then added to the solution. To this clear solution, a catalyst support (metal oxide) was added. The temperature was gradually increased and the pH was continuously monitored using a pH electrode. The initial pH of the reaction mixture (about 2.0 to 2.5) at the initial temperature of 25 °C gradually increased with an increase in the temperature. The final temperature was set to  $98 \pm 2$  °C. The observed final pH was  $8.0 \pm 1.5$ . The solution, which was colored initially (at 25 °C), became almost colorless, after increasing the temperature and pH, indicating the metal chloride was converted into its hydroxide and deposited on the metal oxide support. The solid mass was then filtered, washed thoroughly with deionized water (500 ml x 8 times), air dried at 90 °C for 12 h and then finally calcined at 400 °C for 2 h in static air.

#### ***2.2.3.4 Co-precipitation (CP) Method***

The method was first developed by Haruta and co-workers for the preparation of highly active Au/ $\text{Fe}_2\text{O}_3$ , Au/ $\text{Co}_3\text{O}_4$  and Au/ $\text{NiO}$  catalysts [3]. In this method, the metal nitrate precursor(s) was placed in a three necked round bottom flask and diluted with 200 ml of deionized water. This solution was then heated to 60 °C. The pH and temperature of the solution was monitored continuously. An aqueous gold chloride ( $\text{HAuCl}_4$ ) solution and aqueous solution of  $\text{Na}_2\text{CO}_3$  (0.5 N) was added drop-wise using a burette to the heated solution until the pH of the solution reached 8.0. The stirring was continued for a further 4h at 60 °C. The solution was aged overnight at room temperature, filtered, washed thoroughly with distilled water (500 ml x 8 times), dried at 90 °C for 12 h and finally calcined in air at 400 °C for 2 h.

## **2.2.4 Preparation of Different Metal Oxides**

$\text{Al}_2\text{O}_3$  was prepared by calcining bohemite at 500 °C for 4 h in air oven.  $\text{TiO}_2$ ,  $\text{CeO}_2$ ,  $\text{MoO}_3$  and  $\text{U}_3\text{O}_8$  were prepared by decomposing titanium oxide, cerium nitrate, ammonium molybdate and uranyl nitrate, respectively in muffle furnace at 500 °C for 2 h. All the other metal oxides were procured from the different sources, as given in section 2.1. These metal oxides were heated in air at 400 °C before use. The supported metal oxide catalysts with different metal oxide loadings were prepared by impregnating fine particles of support with corresponding metal nitrates aqueous solution by incipient wetness technique. A weighed quantity of corresponding metal nitrate ( $2 \text{ mmol. g}^{-1}$ ) was first dissolved in minimum amount of deionized water. This was then added to the 2 g support (freshly dried and kept in a desiccator). The mixture was then heated on a water bath to remove the excess of water by evaporation with continuous stirring through out the process of drying. After completely dried, the catalyst was calcined at 500 °C for 3 h under static air. The calcined material was then stored in a desiccator.

## **2.2.5 Preparation of Supported Pd Catalysts**

The supported Pd catalysts were prepared by different methods as follows:

### ***2.2.5.1 Preparation of $\text{PdCl}_2$ Solution***

$\text{PdCl}_2$  (99%, Lancaster Chemicals Ltd., Germany) brown color powder (5.0 g), was dissolved in 5 ml concentrated HCl and aged on boiling water bath (85-95 °C) until the solute was dissolved completely. Deionized water was added to this mother solution to make the volume upto 250 ml. The calculated molarity of the solution was 0.113 M.

### ***2.2.5.2 Impregnation Technique***

In this method, the catalyst was prepared by incipient wetness technique by contacting the metal oxide support (2.0 g) with an aqueous solution of  $\text{PdCl}_2$  containing the required

amount of palladium, evaporating the water on water bath with vigorous stirring and drying at 100 °C for 4 h and then calcined in static air in muffle furnace at 500 °C for 3 h. The presence of PdO phase was confirmed by X-ray diffraction.

The PdO containing catalysts were reduced by treating them with an ammonical hydrazine solution on boiling water bath during which the catalyst color changed from brown to black indicating the phase transformation from PdO to metallic palladium.

#### ***2.2.5.3 Deposition Precipitation (DP) Method***

The PdCl<sub>2</sub> solution containing known amount of Pd was heated under continuous stirring at a temperature of 70 °C. The pH of the solution was adjusted using alkali hydroxide to about 7.0. The metal oxide support (ZrO<sub>2</sub>) was then added to the stirred solution and the pH was again adjusted to about 7.0. The slurry was aged for 1 h, after which it was washed with 4 liter deionized water to remove chlorides and free PdCl<sub>2</sub> from the solution. The resulting material was vacuum dried at 90 °C for overnight and calcined in air at 400 °C for 2 h.

#### ***2.2.5.4 Homogeneous Deposition Precipitation (HDP) Method***

The supported Pd catalysts were prepared by HDP method using urea as a hydrolyzing agent by the procedure similar to that discussed in section 2.2.3.3 except that PdCl<sub>2</sub> was used instead of HAuCl<sub>4</sub>.

#### ***2.2.5.5 Co-Precipitation (CP) Method***

The supported Pd catalysts were prepared by co-precipitation method using Na<sub>2</sub>CO<sub>3</sub> as a hydrolyzing agent by the procedure similar to that discussed in Chapter 2 section 2.2.3.4 except that PdCl<sub>2</sub> was used instead of HAuCl<sub>4</sub>.



## 2.3 CATALYST CHARACTERIZATION

### 2.3.1 X-Ray Diffraction (XRD)

The XRD studies of the selected catalysts were carried out using a Holland Philips, PW/1730 X-ray generator with CuK $\alpha$  radiation scintillation counter. The samples were prepared as a thin layer on a glass slide. XRD analysis was performed to identify the crystal phases of the metal oxide and gold. The identification of the catalysts crystalline phase was performed by, comparing the 2 $\theta$  values of XRD peaks with those of standard XRD values. In order to determine the particle size of the gold using XRD, a 100 % peak of Au (111) at 38.2 °C was considered and Scherer's equation was used as follows:

$$D = \frac{0.9\lambda}{\beta \times \pi / 180 \times \cos \theta}$$

Where,  $\lambda$  = wavelength of the X-ray used (for Cu K $\alpha$  radiation,  $\lambda = 1.5406 \text{ \AA}$ ),  $\beta$  = Full width at half maximum,  $\theta$  = Bragg's diffraction angle and  $D$  = particle size in  $\text{\AA}$ . The corrected  $\beta$  value was determined by the following relation:  $\beta = \sqrt{[\beta^2_{(\text{experimental})} - \beta^2_{(\text{instrumental})}]}$

### 2.3.2 Surface Area

The surface area of the catalysts were measured by a single point BET method by measuring the adsorption of nitrogen at a concentration of 30 mole % N $_2$  in He, using a Monosorb Surface Area Analyzer (Quantachrome Corp., USA) based on the dynamic adsorption/desorption technique.

Before carrying out surface area measurements, the catalyst was pretreated *in-situ* in the sample cell at 200 °C for 1 h in a flow (30 cm $^3$ .min $^{-1}$ ) of N $_2$ -He mixture (30 mole % N $_2$ ) to remove the traces of moisture.

The analyzer was calibrated by injecting a known amount of air. The surface area was calculated from the observed desorption counts.

$$\text{Surface area (m}^2\cdot\text{g}^{-1}\text{)} = (\text{Desorption counts} \times 2.84) / (\text{Wt. of catalyst} \times \text{Counts of 1 ml of air}).$$

### **2.3.3 Induced Coupling Plasma (ICP) Analysis**

ICP-OES (Perkin Elmer Analyzer) was used for bulk elemental chemical analysis. ICP analysis of gold containing catalysts was performed as follows: 50 mg of catalyst was dissolved in 5 ml of aquaregia. The solution was left for 30 minute to dissolve all solids and filtered. Deionized water was used to wash the filter assembly and glassware in order to remove all gold from the glasswares. The filtrate was then collected in a 25 ml volumetric flask and diluted with deionized water.

### **2.3.4 X-Ray Photoelectron Spectroscopy (XPS)**

Surface chemical analysis of the catalyst was carried out using an X-ray photoelectron spectroscopy (XPS) using a VG-Scientific ESCA-3 MK-II electron spectrometer (C1s with binding energy = 285.0 eV) was used as internal standard. The electron binding energies (with accuracy of 0.2 eV) were determined from the observed kinetic energies using the relation, Binding energy (B.E.) =  $h\nu$  - kinetic energy (K. E.).

The X-ray radiation ( $h\nu$ ) used in the XPS was Mg  $K\alpha$  (1253.6 eV).

The atom ratio of two elements (A and B) on the catalyst surface was determined from the XPS peaks as follows:

$$\text{A/B atom ratio} = [\text{peak area of A}/\text{photo ionization cross section of A}]/[\text{peak area of B}/\text{photo ionization cross section of B}].$$

### **2.3.5 Transmission Electron Microscopy (TEM)**

TEM analysis was done using a JEOL (Model No. JEM 1200 EX). The sample was prepared from an acetone suspension of solid sample by placing a drop of the sample solution on a carbon coated copper grid. It gives structure, size, shape and the distribution of phases that make up a material.

### **2.3.6 Nuclear Magnetic Resonance (NMR)**

NMR is a physical phenomenon based upon the quantum mechanical magnetic properties of an atom's nucleus. All nuclei that contain odd numbers of protons or neutrons have an intrinsic magnetic moment and angular momentum. The most commonly measured nuclei are hydrogen-1 (the most receptive isotope at natural abundance) and carbon-13, although nuclei from isotopes of many other elements can also be observed. NMR studies of magnetic nuclei by aligning them with a very powerful external magnetic field and perturbing this alignment using an electromagnetic field. The resulting response to the external perturbing electromagnetic field is the phenomenon that is exploited in nuclear magnetic resonance spectroscopy and magnetic resonance imaging.

The NMR spectroscopy is one of the principal techniques used to obtain physical, chemical, electronic and structural information about molecules. It is a powerful technique that can provide detailed information on the topology, dynamics and three-dimensional structure of molecules in solution and the solid state.  $^1\text{H}$  NMR spectra and  $^{13}\text{C}$  NMR were determined on a Bruker AC-200, 300, 400 or 500 spectrometer (200, 300, 400 or 500 MHz) with TMS as the internal standard.

### **2.3.7 Fourier Transform Infrared Spectroscopy (FTIR)**

Fourier transform infrared (FTIR) spectra of samples were recorded on an ATI MATTSON RS-1 FTIR spectrometer. FTIR spectra of the catalysts in the framework region

(450-4000  $\text{cm}^{-1}$ ) were obtained in KBr disc or in nujol film. The atoms in a molecule do not remain in a fixed relative position and vibrate about some mean position. Due to this vibrational motion, if there is a periodic alternation in the dipole moment then such mode of vibration is infrared (IR) active. The IR region of the electromagnetic spectrum is 100-1 $\mu\text{m}$  wavelength. The vibrating molecule absorbs energy only from radiation with which it can coherently interact, i.e. the radiation of its own oscillation frequency. The appearance or non-appearance of certain vibrational frequencies gives valuable information about the structure of a particular molecule. Each functional group have specific range of vibrational frequencies and are very sensitive to the chemical environment and the neighbouring, thus provide valuable information regarding the presence of certain functional groups in the specific sample for their further characterization and identification.

### **2.3.8 Mass Spectrometry**

It is a technique that allows to measure the molecular weight of a substance. Mass spectra were determined on API-QSTAR Pulsar Mass Spectrometer. Mass Spectrometer is an instrument, which produces a beam of gaseous molecular ions from a substance. It sorts out the ions according to their mass to charge ratio ( $m/z$  or  $m/e$ ) and record their masses and relative abundances.

### **2.3.9 Elemental Analysis**

The exact composition of the materials and their molecular formula were estimated from elemental analysis (C, H & N). The C, H & N analyses of the samples were done on a FLASH EA 1112 SERIES-CHNS elemental analyzer. In a typical analysis, about 3-5 mg of sample was used to estimate the percentage of C, H and N contents.

## 2.4 CATALYTIC REACTIONS

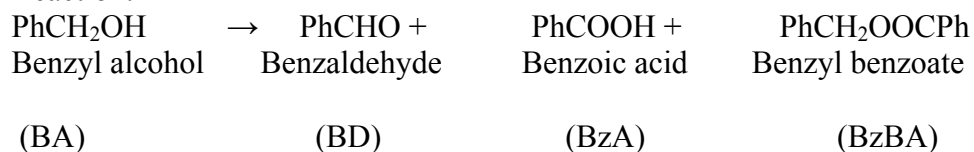
### 2.4.1 Oxidation of Benzyl Alcohol

The catalytic oxidation of benzyl alcohol was carried out in a magnetically stirred round bottom flask (capacity: 25 cm<sup>3</sup>), provided with a mercury thermometer for measuring the reaction temperature and reflux condenser as shown in Figure 2.1, at the following reaction conditions [reaction mixture = 52 mmol benzyl alcohol + 78 mmol TBHP (70 % TBHP in water) + 0.5 g catalyst, temperature = 92-95 °C (under reflux at a bath temperature of 97 °C), reaction time = 1-10 h].

The reaction products were analyzed by gas chromatography with flame ionization detector, using a SE-30 column and N<sub>2</sub> as a carrier gas.

The conversion, yield and selectivity were calculated by following equations.

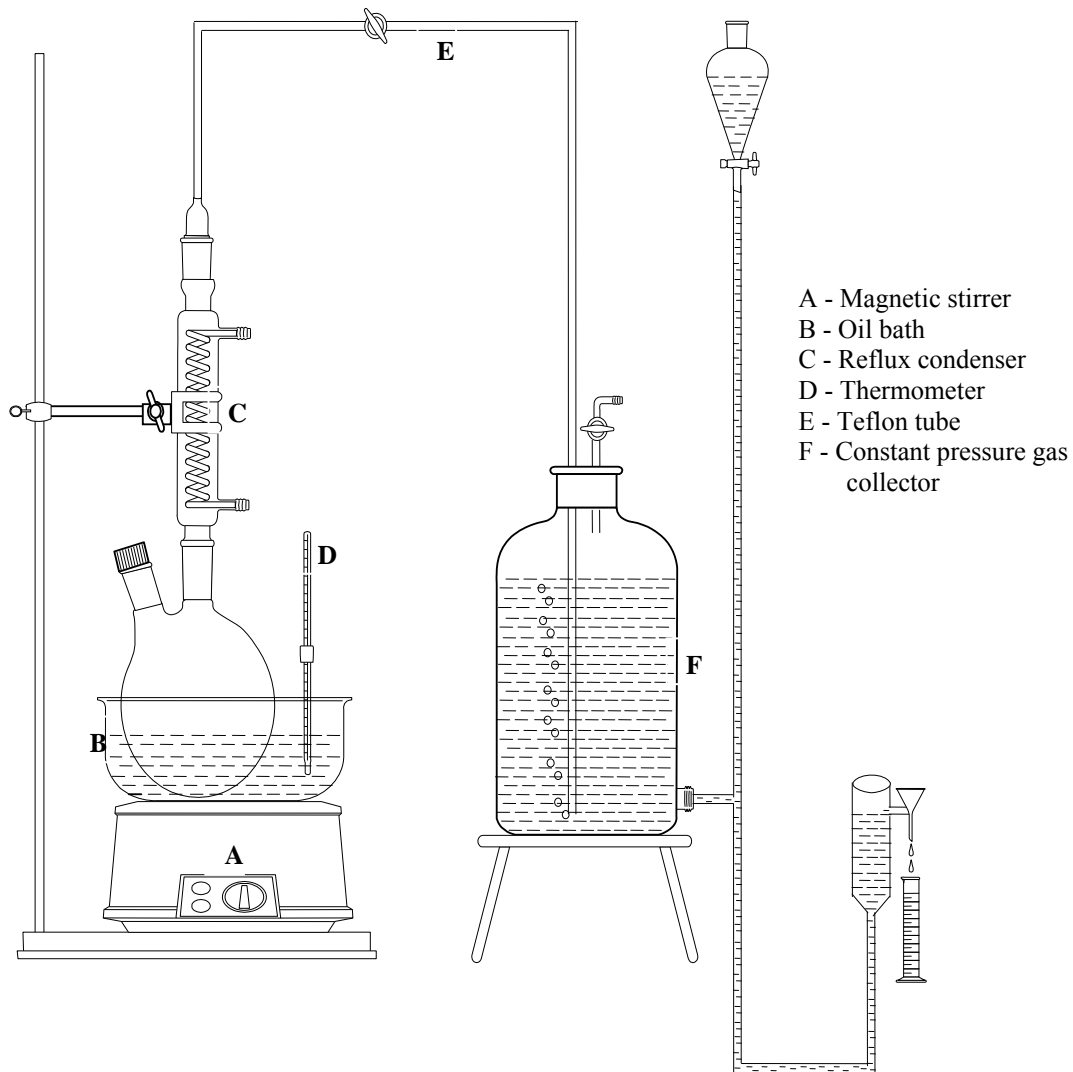
Reaction:



Conversion of BA (%) =  $[\{(\text{amount of BA})_{\text{at } t=0} - (\text{amount of BA})_{\text{at } t=t}\} \div (\text{amount of BA})_{\text{at } t=0}] \times 100$ .

Yield of BD (%) =  $[(\text{amount of BD})_{\text{at } t=t} \div (\text{amount of BA})_{\text{at } t=0}] \times 100$ .

Selectivity of BD (%) =  $[\{\text{yield of BD (\%)}\} \div \{\text{Conversion of BA (\%)}\}] \times 100$ .



**Figure 2.1** Set-up for the oxidation of Benzyl alcohol

#### 2.4.2 Heck Arylation of Olefins

The Heck arylation of different olefins with aryl halides was carried out in a magnetically stirred round bottom flask (capacity = 25 cm<sup>3</sup>), provided with a mercury thermometer for measuring the reaction temperature and reflux condenser, as shown in Figure 2.2, at the following reaction conditions: [reaction mixture = 2.5 mmol aryl halide + 6.5 mmol, olefin + 5 ml solvent + 1 g base + catalyst (10 wt % of aryl halide), nitrogen (10 ml/min), bath temperature = 140 °C].

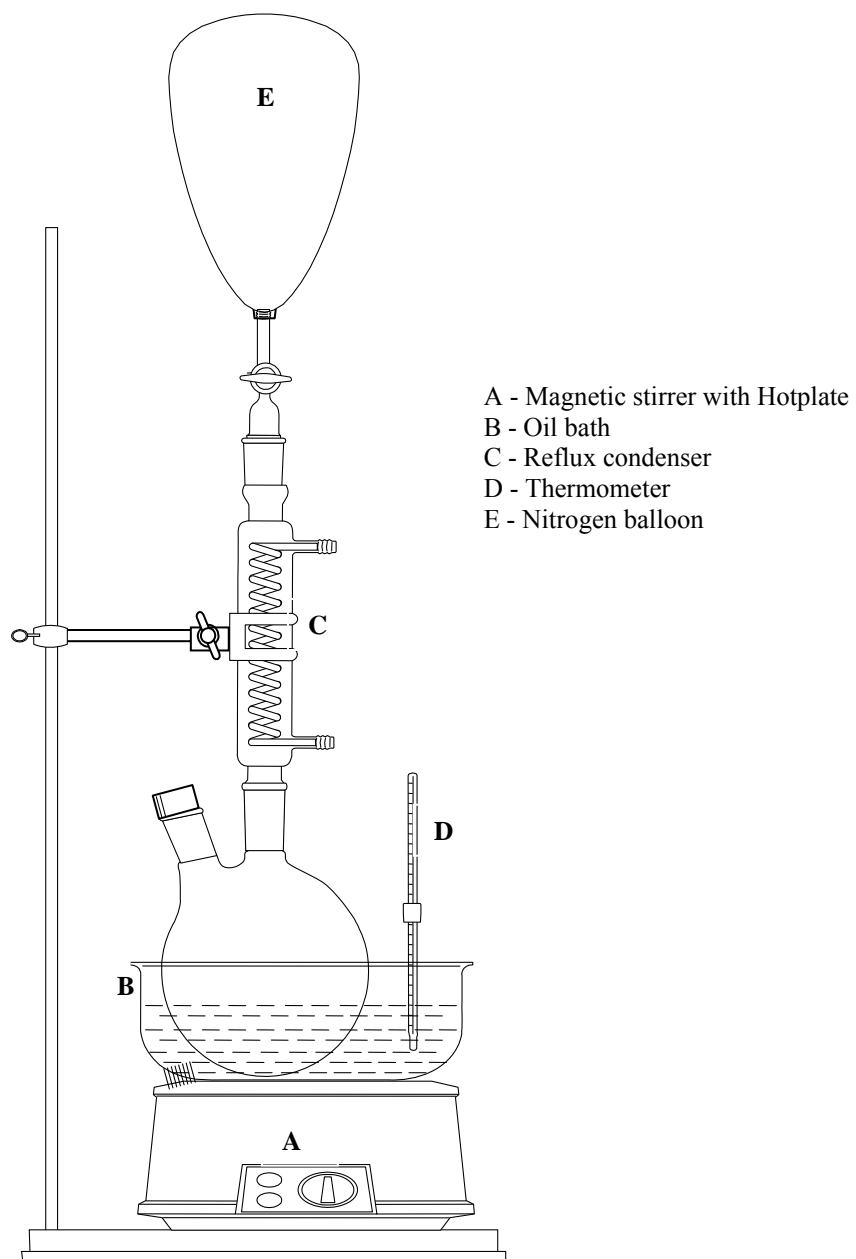
The Heck reaction was monitored by TLC. After completion of reaction, the catalyst was separated by filtration and washed with DMF (3 x 3 ml). Then the filtrate was diluted with water followed by extraction with ethyl acetate to obtain the crude product, which was subsequently purified by column chromatography on silica gel with petroleum ether/ethyl acetate as eluent. The catalyst was further washed with acetone, dried and reused. The reaction products were isolated by column chromatography and were confirmed by NMR, IR, Mass spectroscopy and elemental analysis.

The isolated product yield was defined as follows:

$$\text{Product yield (\%)} = [\text{moles of isolated product}] \div [\text{moles of aryl halide used}] \times 100$$

#### 2.4.3 Ullmann Reaction of Aryl halides for the Formation of Biaryls

The Ullmann Reaction of aryl halide was carried out in a magnetically stirred round bottom flask (capacity = 25 cm<sup>3</sup>), provided with a mercury thermometer for measuring the reaction temperature and reflux condenser as shown in Figure 2.2, at the following reaction conditions: [reaction mixture = 2.5 mmol aryl halide (with or without 2.5 mmol of second aryl halide) + 5 ml solvent + 0.5 g base + catalyst (10 wt % of aryl halide), nitrogen (10 ml/min), bath temperature = 140 °C].



**Figure 2.2** Set-up for the Heck reaction and Ullmann reaction



The Ullmann reaction was also monitored by TLC and subsequently crude product was purified by column chromatography. The reaction products were isolated by column chromatography and were confirmed by NMR and IR spectroscopy. The isolated yield was calculated by the following equation.

$$\text{Yield of product (\%)} = [\text{moles of isolated product}] \div [\text{moles of aryl halide used}] \times 100.$$

## 2.5 REFERENCES

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- [2] S. Tsubota, M. Haruta, T. Kobayashi, A. Ueda and Y. Nakahara, *Stud. Surf. Sci. Catal.*, 72 (1991) 695.
- [3] M. Haruta, N. Yamada, T. Kobayashi and S. Lijima, *J. Catal.*, 115 (1989) 301.

## **CHAPTER-3**

**Solvent-free Selective Oxidation of Benzyl Alcohol by TBHP to Benzaldehyde Using Solid Catalysts Derived from Hydrotalcite, Layered Double Hydroxides or Mixed Metal Hydroxides**

## CHAPTER-3

# Solvent-free Selective Oxidation of Benzyl Alcohol by TBHP to Benzaldehyde Using Solid Catalysts Derived from Hydrotalcite, Layered Double Hydroxides or Mixed Metal Hydroxides

### 3.1 BACKGROUND AND OBJECTIVE OF PRESENT WORK

Selective oxidation of benzyl alcohol to benzaldehyde is a practically important reaction for the production of chlorine free benzaldehyde required in perfumery and pharmaceutical industries. Several studies have been reported on the catalytic vapor phase oxidation of benzyl alcohol to benzaldehyde [1]. However, in the vapor phase oxidation, carbon oxides are also formed, leading to significant carbon loss. Liquid phase oxidation of benzyl alcohol to benzaldehyde is, therefore, preferable. A few studies have been reported on the liquid phase oxidation of benzyl alcohol by oxygen or aqueous  $H_2O_2$  in the presence of different solvents, using Pd/C [2], Pd-Ag/pumice [3], heteropolyacid [4] and Ni-Al-hydrotalcite [5] catalysts.

Recently, Kotai et. al. [6] have reported the formation of benzaldehyde, ammonia and  $MnO_2$  by the stoichiometric reaction between ammonium permanganate and benzyl alcohol at room temperature. The oxidation of benzyl alcohol to benzaldehyde and benzoic acid using stoichiometric or excess amounts of potassium permanganate in aqueous acidic medium has also been reported earlier [7]. These stoichiometric reactions have severe limitations, such as the formation of a large amount of liquid/solid wastes and corrosive nature of the acidic reaction medium.

Recently, Choudhary et. al. [8] have reported different layered double hydroxides (LDHs) as active and highly selective catalysts for the benzyl alcohol oxidation using

molecular oxygen as an oxidant. It is interesting to use these catalysts for the benzyl alcohol to benzaldehyde oxidation by TBHP. The photocatalytic oxidation of benzyl alcohol by 9-phenyl-10-methylacridinium [9] and by an artificial enzyme [10] has also been reported.

The choice of an oxidant mainly depends on two factors; (1) the nature of the corresponding by-product and (2) the active-oxygen content in the oxidant (besides price and ease of handling). The first factor is most important for environmental reasons, while the later one influences the productivity of the process. However, among all the oxidizing agents, molecular oxygen is the most attractive option, but due to much lower reactivity restricts its applicability mostly to high temperature reactions. Apart from this, O<sub>2</sub>/organic vapor mixtures may sometimes spontaneously ignite, leading to explosion hazards. Then aqueous H<sub>2</sub>O<sub>2</sub> is another attractive option having high active oxygen content and water (which is environmentally benign) is the only by-product. However, the inherent co-production of water poses some serious difficulties because most of the transition metal based catalysts are very sensitive to water, which may cause leaching of their active metal component from the catalyst and also have retarding effect on some reactions. Hence, organic hydro peroxides are the commonly used oxidants for catalytic liquid phase oxidation. The use of organic hydro peroxide generates stoichiometric amounts of corresponding tertiary alcohol, which can be removed easily by simple distillation. The resulting tertiary alcohol acts as a solvent during the oxidation.

It is of both scientific and practical interests to use different hydrotalcite clay-like materials such as layered double hydroxides (LDHs) containing different transition metals as well as permanganate in the catalytic amounts for the liquid phase oxidation of benzyl alcohol to benzaldehyde, using an oxidizing agent such as *tert*-butylhydroperoxide (TBHP).

The present study was undertaken with the objective of investigating the performance of  $\text{MnO}_4^{-1}$ -exchanged Mg-Al-hydrotalcites and different synthetic hydrotalcite-like materials, such as LDHs containing one or two different transition elements (viz. Ni, Co, Zn, Cu, Fe, Mn, and Cr), as the catalyst in the solvent-free liquid phase selective oxidation of benzyl alcohol to benzaldehyde by *tert*-butylhydroperoxide (TBHP). These catalysts were also used for the selective oxidation of benzaldehyde to benzoic acid.

### 3.2 CATALYSTS AND BRIEF EXPERIMENTAL PROCEDURES

The  $\text{MnO}_4^{-1}$ -exchanged ( $\text{MnO}_4^{-1}$  loading =  $0.42 \pm 0.01$  mmol.  $\text{g}^{-1}$ ) Mg-Al-hydrotalcite catalysts with Mg/Al ratio of 2, 3, 5 and 10 were prepared as follows. Mg-Al-hydrotalcite was synthesized by adding two aqueous solutions, one containing magnesium nitrate and aluminium nitrate with required Mg/Al ratio and second containing potassium hydroxide and potassium carbonate dropwise, into a flask containing deionized water under vigorous stirring at 40 °C, while maintaining a constant pH of 11-12, by the procedure similar to that of described earlier [11]. The resulting white gel was aged for 0.5 h, filtered, thoroughly washed and then dried at 80 °C in vacuum oven for 12 h. In these hydrotalcites,  $\text{MnO}_4^{-1}$  anions were incorporated as follows. The resulting Mg-Al-hydrotalcite was powdered and calcined at 600 °C for 4 h. The calcined mass (13 g) was then treated under stirring with an aqueous solution of  $\text{KMnO}_4$  (1.58 g in 100 ml water), at 80 °C for 24 h. The resulting  $\text{MnO}_4^{-1}$ -exchanged Mg-Al-hydrotalcite was filtered and washed with hot deionized water and then dried at 80 °C in vacuum oven. The amount of  $\text{MnO}_4^{-1}$ -exchanged was determined by analyzing the amount of  $\text{KMnO}_4$  present in the filtrate and washing. Before using, the  $\text{MnO}_4^{-1}$ -exchanged Mg-Al-hydrotalcite catalysts

were heated in an air oven at 200 °C for 2 h. The LDH catalysts were prepared by the procedures described earlier (Chapter 2, Section 2.2.1).

The catalysts were characterized for their crystalline phase(s) by XRD [using a Phillips Diffractometer (1730 series) and  $\text{CuK}_\alpha$  radiations], for their surface area by the single point  $\text{N}_2$  adsorption method (using a Surface Area Analyser; Quanta Chrome, USA) and also for their basicity by measuring the pH of their suspension in water (0.15 g catalyst in 10 ml deionized water at room temperature) and also for their  $\text{CO}_3^{2-}$  content (by treating the catalyst with 4.0 M  $\text{HNO}_3$  and measuring quantitatively the  $\text{CO}_2$  evolved). The catalysts were also characterized by Fourier Transform Infrared (FTIR) spectroscopy and the samples were recorded on an ATI MATTSON RS-1 FTIR spectrometer. FTIR spectra of the catalysts in the framework region ( $450\text{-}4000\text{ cm}^{-1}$ ) were obtained in KBr disc or in nujol film.

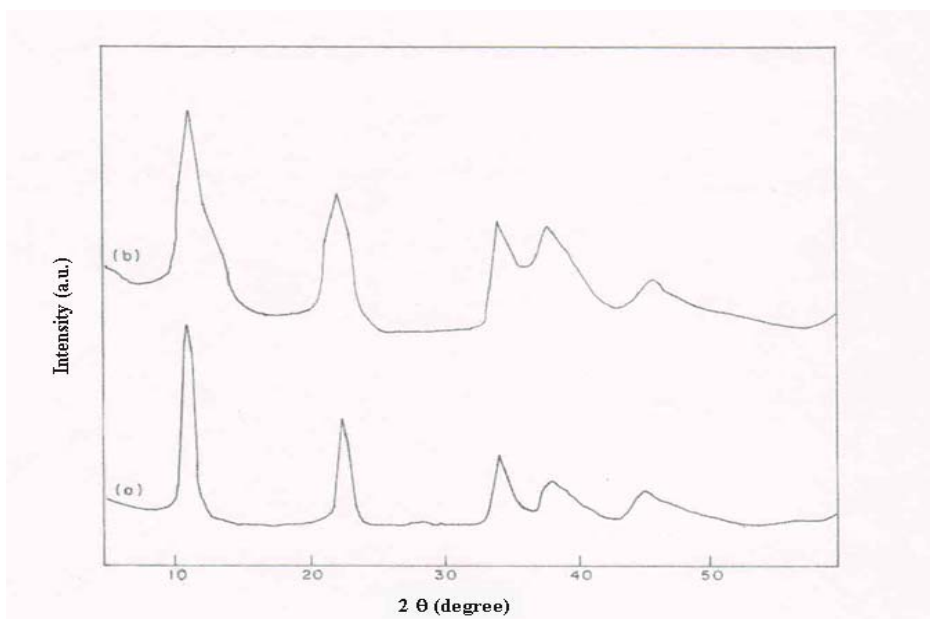
The catalytic oxidation of benzyl alcohol was carried out in a magnetically stirred round bottom flask (capacity: 25  $\text{cm}^3$ ), provided with a mercury thermometer for measuring the reaction temperature and reflux condenser as already shown in Figure 2.1, at the following reaction conditions: reaction mixture = 52 mmol benzyl alcohol + 78 mmol TBHP (70 % TBHP in water) + 0.5 g catalyst, temperature = 92-95 °C (under reflux at a bath temperature of 97 °C), reaction time = 1-10 h. The reaction products were analyzed by gas chromatograph with flame ionization detector, using a SE-30 column and  $\text{N}_2$  as a carrier gas.

### **3.3 BENZYL ALCOHOL TO BENZALDEHYDE OXIDATION OVER $\text{MnO}_4^{-1}$ -EXCHANGED Mg-Al-HYDROTALCITE**

#### **3.3.1 Characterization of $\text{MnO}_4^{-1}$ -exchanged Mg-Al-HT**

The Mg-Al-hydrotalcites and  $\text{MnO}_4^{-1}$ -exchanged Mg-Al-hydrotalcite catalysts were characterized for their crystalline structure by XRD (Figure 3.1). The XRD results showed that,

after the  $\text{MnO}_4^{-1}$ -exchanged, the hydrotalcite structure remained intact as indicated by the presence of hydrotalcite phase in the catalyst. The catalysts were also characterized by Infrared spectroscopy. From the results following important observations can be made.



**Figure 3.1:** XRD spectra of a) 3Mg-Al-hydrotalcite, b)  $\text{MnO}_4^{-1}$ -3Mg-Al-HT (before the oxidation reaction), ( $\text{MnO}_4^{-1}$ -exchanged =  $0.42 \text{ mmol.g}^{-1}$ ).

- The appearance of an IR band in the region  $890 \text{ cm}^{-1}$ ,  $920 \text{ cm}^{-1}$  after exchanging the hydrotalcite with aqueous  $\text{KMnO}_4$  indicated the presence of  $\text{MnO}_4^{-1}$  anions in the  $\text{MnO}_4^{-1}$ -exchanged hydrotalcite catalysts [12].
- The  $\text{MnO}_4^{-1}$ -exchanged hydrotalcites were treated with an aqueous sodium carbonate solution, a quantitative replacement of the exchanged  $\text{MnO}_4^{-1}$  anions by carbonate anions were observed.

These observations clearly show that, in the  $\text{MnO}_4^{-1}$ -exchanged hydrotalcite catalysts, the  $\text{MnO}_4^{-1}$  anions are located at the anion-exchange positions in the hydrotalcite catalysts.

Data on characterization of the  $\text{MnO}_4^{-1}$ -exchanged Mg-Al-hydrotalcite catalysts with different Mg/Al ratios are presented in Table 3.1. The large amount of  $\text{CO}_2$  evolved in the acidification of the catalysts indicates that the anions present in the hydrotalcite catalysts other than  $\text{MnO}_4^{-1}$  anions are carbonated anions. The pH ( $> 7.0$ ) of the catalyst-water suspension is an indication of basic nature of the catalysts.

**Table 3.1** Characterization of  $\text{MnO}_4^{-1}$ -exchanged Mg-Al-hydrotalcite catalysts with different Mg/Al ratios

Mg/Al ratio	Conc. of $\text{MnO}_4^{-1}$ anions ( $\text{mmol.g}^{-1}$ )	XRD phase	Surface area ( $\text{m}^2.\text{g}^{-1}$ )	$\text{CO}_2$ evolved in the acid treatment ( $\text{mmol. g}^{-1}$ )	pH of the suspension of catalyst in water
2.0	0.42	HT <sup>a</sup>	36.3	2.15	9.3
3.0	0.40	HT <sup>a</sup>	31.5	1.74	9.8
5.0	0.41	HT <sup>a</sup>	29.1	1.29	10.0
10.0	0.40	HT <sup>a</sup>	25.9	0.84	10.4

<sup>a</sup>Hydrotalcite phase

The basicity of the hydrotalcite catalysts were studied by titrating them with non-aqueous benzoic acid using a phenolphthalein indicator ( $\text{pK}_a= 9.3$ ) [13] and/or by measuring the pH of their suspension in water (0.15 g solid particles in 10 ml deionized water at 27 °C). The increase in the pH with increasing the Mg/Al ratio suggests that the basicity of the catalyst is increased with increasing the Mg/Al ratio. The surface area of the catalyst is, however, decreased with increasing the Mg/Al ratio. The surface area of the resulting Mg-Al-hydrotalcite with Mg/Al ratio of 2, 3, 5 and 10 was 60.3, 57.8, 76.8 and 70.7  $\text{m}^2.\text{g}^{-1}$ , respectively. The surface area of the catalyst was however not changed significantly after the reaction.



### 3.3.2 Oxidation of CH<sub>2</sub>OH Group of Aromatic Compounds over MnO<sub>4</sub><sup>-1</sup>-exchanged Mg-Al-Hydrotalcites

The performances of MnO<sub>4</sub><sup>-1</sup>-exchanged hydrotalcite catalysts on oxidation of benzyl alcohol by TBHP are presented in Table 3.2.

**Table 3.2:** Results of the oxidation of benzyl alcohol to benzaldehyde by TBHP over the MnO<sub>4</sub><sup>-1</sup>-exchanged Mg-Al-hydrotalcite with different Mg/Al ratios and KMnO<sub>4</sub> [reaction conditions: reaction mixture = 52 mmol benzyl alcohol + 78 mmol TBHP (70 % TBHP in water) + 0.5 g catalyst, temperature = 92-95 °C (under reflux at a bath temperature of 92-95 °C), reaction time = 5 h].

Mg/Al ratio	Conversion of benzyl alcohol (%)	Selectivity (%)		
		Benzaldehyde	Benzoic acid	Benzyl benzoate
2	35.2	99.8	0.2	0.0
3	37.4	98.6	0.1	1.3
3 <sup>a</sup>	29.5	99.5	0.05	0.5
5	45.3	98.4	0.04	1.5
10	50.2	99.7	0.3	0.0
10 <sup>b</sup>	4.7	100	0.0	0.0
KMnO <sub>4</sub> <sup>c</sup>	28.5	84.4	14.4	1.2
Without any catalyst	14.3 <sup>d</sup>	99.0	1.0	0.0

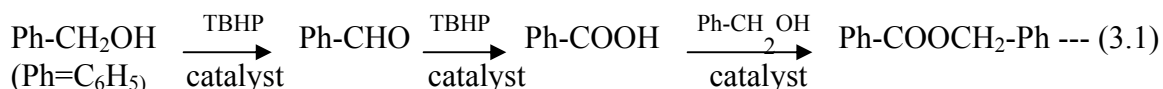
<sup>a</sup>MnO<sub>4</sub><sup>-1</sup>-exchanged Mg-Al-HT (Mg/Al = 3) was attained by directly exchanging the Mg-Al-HT with KMnO<sub>4</sub> solution under identical conditions (amount of MnO<sub>4</sub><sup>-1</sup>-exchanged = 0.104 mmol g<sup>-1</sup>). <sup>b</sup>Mg-Al-hydrotalcite (Mg/Al = 10) without MnO<sub>4</sub><sup>-1</sup> anions. <sup>c</sup>Fine particles of KMnO<sub>4</sub> equivalent to that present in the MnO<sub>4</sub><sup>-1</sup>-exchanged Mg-Al hydrotalcite catalysts (the reaction mixture was colorless). <sup>d</sup>Conversion due to non-catalytic homogeneous reaction.

It is interesting to note that, although the concentration of  $\text{MnO}_4^{-1}$  anions in the hydrotalcite catalysts is nearly the same, the activity of the catalyst showed a strong dependence upon its Mg/Al ratio; the activity is increased with increasing the Mg/Al ratio. This may be attributed to the different basicities of the hydrotalcite catalysts; higher the basicity, higher is the catalytic activity (Tables 3.1 and 3.2).

It is also interesting to note that the conversion of benzyl alcohol in the absence of any catalyst (14.3 %) is higher than that (4.7 %) in the presence of the Mg-Al-HT (Mg/Al = 10) without containing  $\text{MnO}_4^{-1}$  anions. Thus, in the absence of  $\text{MnO}_4^{-1}$  anions, the hydrotalcite inhibits the oxidation reaction, most probably because of the termination of radical intermediates (formed in the homogeneous oxidation) by the hydrotalcite.

The  $\text{MnO}_4^{-1}$ -exchanged Mg-Al-HT is an active catalyst for the selective oxidation of benzyl alcohol to benzaldehyde in the absence of any solvent. Its catalytic activity and selectivity is much higher than that of  $\text{KMnO}_4$  alone (i.e. when  $\text{KMnO}_4$  in the form of fine particles was used instead of the hydrotalcite catalyst). This is expected mostly because of the highly dispersed  $\text{MnO}_4^{-1}$  anions in the hydrotalcite catalyst.

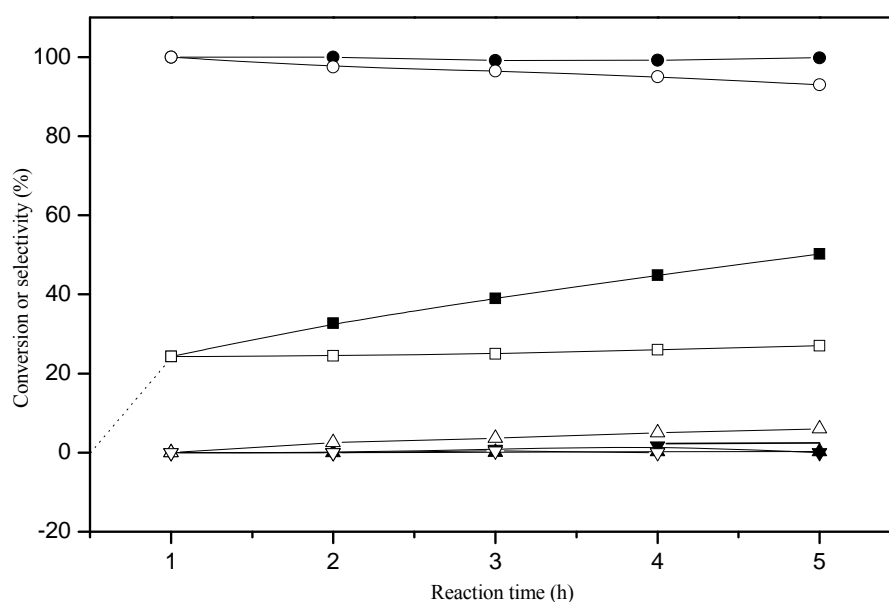
From the observed products, the consecutive reactions involved in the benzyl alcohol oxidation can be schemated as follows:



It is also interesting to note (from Table 3.2) that, the direct exchange of  $\text{MnO}_4^{-1}$  anions with Mg-Al-HT leads to a less active catalyst than that obtained from the thermally decomposed hydrotalcite (Table 3.2), using its memory effect [14].

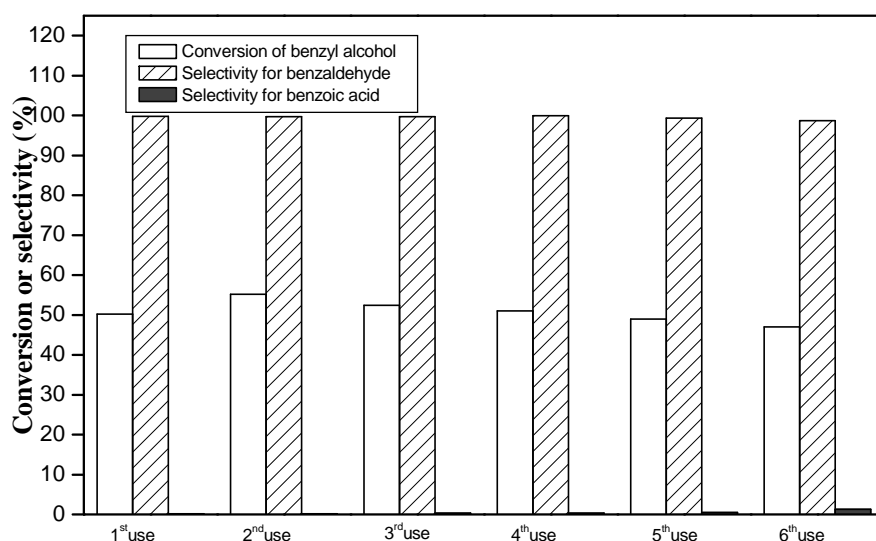
The results in Figure 3.2 clearly show that the benzyl alcohol oxidation reaction is a heterogeneous reaction catalyzed by the solid catalyst. In the presence of the hydrotalcite solid

catalyst, the benzyl alcohol conversion increased continuously without a significant change in the product selectivity with increasing the reaction period. However, when the solid catalyst was removed from the reaction mixture after the reaction period of 1h, the increase in the conversion with the reaction time was very small but there was a significant decrease and increase in the selectivity of benzaldehyde and benzoic acid, respectively. The small increase in the benzyl alcohol conversion is expected because of the non-catalytic oxidation.



**Figure 3.2:** Variation of conversion and product selectivity with the reaction time in the oxidation of benzyl alcohol over  $\text{MnO}_4^-$ -exchanged Mg-Al-hydrotalcite (Mg/Al = 10) catalyst [(■, ●, ▲ and ▼) data in the presence of solid catalyst throughout the reaction for 5 h and (□, ○) data when the solid catalyst was removed from the reaction mixture after the reaction period of 1h. ■ and □: conversion of benzyl alcohol, ● and ○: selectivity for benzaldehyde, ▲, Δ selectivity for benzoic acid, and ▼, ▽ selectivity for benzyl benzoate].

In order to test the catalyst reusability, the  $\text{MnO}_4^-$ -exchanged hydrotalcite catalyst ( $\text{Mg}/\text{Al} = 10$ ) was reused in the benzyl alcohol oxidation several times. The results showing the reusability of the catalyst are presented in Figure 3.3. It is interesting to note that the catalyst performance, particularly the benzyl alcohol conversion, is increased significantly after the first use of the catalyst. The improvement in the performance of the catalyst in its subsequent reuse in the oxidation reaction is probably due to the removal of moisture from the catalyst.

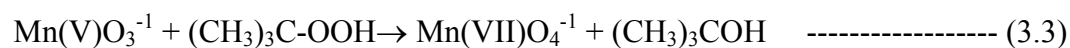
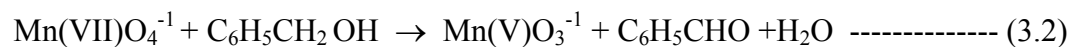


**Figure 3.3:** Reusability of the  $\text{MnO}_4^-$ -exchanged Mg-Al-hydrotalcite ( $\text{Mg}/\text{Al}=10$ ) catalyst in the oxidation of benzyl alcohol (Reaction period = 5h).

It is interesting to note that benzyl benzoate is the only other product formed apart from major product benzaldehyde and there was only a little or no formation of benzoic acid. It seems that, as soon as benzoic acid is formed, it reacts immediately with benzyl alcohol, which is available in much higher concentration, forming benzyl benzoate.

When a mixture of 0.2 ml benzyl alcohol, 6 ml toluene (a solvent) and 1.0 g  $\text{MnO}_4^-$ -exchanged hydrotalcite ( $\text{Mg}/\text{Al} = 10$ ) catalyst was refluxed in the absence of  $\text{O}_2$  and/or TBHP

for a period of 5 h, there was a significant conversion of benzyl alcohol (7.5 %) to benzaldehyde. The conversion is expected mainly due to the stoichiometric liquid-solid reaction between the  $\text{MnO}_4^{-1}$  anions of the catalyst and the substrate (benzyl alcohol). This indicates a high possibility of the operation of a redox mechanism in the above oxidation reaction in the presence of TBHP, involving following redox reactions:



Reaction (3.2) is expected to be the rate-limiting step in the oxidation. The basic sites of the catalyst may be responsible for the activation of benzyl alcohol through partial abstraction of H from its  $-\text{CH}_2-$  group.

### 3.3.3 Oxidation of Benzaldehyde to Benzoic Acid

The  $\text{MnO}_4^{-1}$ -exchanged hydrotalcites with different Mg/Al ratios have also been evaluated for the oxidation of benzaldehyde by TBHP in the absence of any solvent. Results showing the selective oxidation of benzaldehyde to benzoic acid by TBHP over the  $\text{MnO}_4^{-1}$ -exchanged hydrotalcites with different Mg/Al ratios are given in Table 3.3. Like in the case of benzyl alcohol oxidation, in this case also the conversion is increased with increasing the Mg/Al ratio; there was no formation of product other than benzoic acid. The catalyst, particularly the one with Mg/Al=10, shows high activity for the selective oxidation of benzaldehyde to benzoic acid.

**Table 3.3:** Results for the oxidation of benzaldehyde to benzoic acid by TBHP over  $\text{MnO}_4^-$ -exchanged Mg-Al-hydrotalcite with different Mg/Al ratios [reaction conditions: reaction mixture = 50 mmol benzaldehyde + 78 mmol TBHP + 0.5 g catalyst, temperature = under reflux (bath temperature = 92-97 °C), reaction time = 5 h].

Mg/Al ratio	Conversion of benzaldehyde (%)	Selectivity for benzoic acid (%)
2	84.2	100
3	92.7	100
5	94.5	100
10	99.4	100

### 3.4 BENZYL ALCOHOL TO BENZALDEHYDE OXIDATION OVER TRANSITION METAL CONTAINING LAYERED DOUBLE HYDROXIDES (LDHs) AND/OR MIXED HYDROXIDES CATALYSTS

Since the  $\text{MnO}_4^-$ -exchanged Mg-Al-hydrotalcite catalyst showed highly promising performance in the solvent-free liquid phase selective oxidation of benzyl alcohol to benzaldehyde by *tert*-butylhydroperoxide (TBHP), it was interesting to carry out further investigation using various layered double hydroxides (LDHs) containing different transition metal of divalent [M (II)] and trivalent [M (III)] metallic elements (viz. Mn-Al, Co-Al, Ni-Al, Zn-Al, Mg-Fe, Mn-Fe, Co-Fe, Ni-Fe, Mn-Cr, Co-Cr, Ni-Cr, Cu-Cr, and Zn-Cr etc.) for the oxidation reaction. Influence of the different reaction conditions (reaction time and reaction temperature) on the catalytic performance of the layered double hydroxides (LDHs) catalysts

has also been investigated. The layered double hydroxides (LDHs) catalysts were prepared by the procedure described earlier (Chapter 2, Section 2.2.1).

### **3.4.1 Characterization of Layered Double Hydroxide (LDH) and/or Mixed Metal Hydroxide (MMH) Catalysts**

The LDH and MMH solid materials were characterized for their crystalline phase(s) by XRD, for their surface area, also for their basicity by measuring the pH, for their  $\text{CO}_3^{2-}$  content and also for their  $\text{H}_2\text{O}_2$  decomposition activity by determining the time required for half the  $\text{H}_2\text{O}_2$  decomposition.

The  $\text{H}_2\text{O}_2$  decomposition over the LDHs was carried out in a magnetically stirred glass reactor (capacity 25  $\text{cm}^3$ ) at 27 °C by injecting 1.0 ml of aqueous  $\text{H}_2\text{O}_2$  (30 %) solution in the reactor containing 10 ml distilled water and 0.1g catalyst and measuring quantitatively the amount of oxygen evolved in the decomposition ( $\text{H}_2\text{O}_2 \rightarrow 0.5 \text{O}_2 + \text{H}_2\text{O}$ ) using constant pressure gas collector [15].

The results of the characterization of the LDH catalysts are presented in Table 3.4 where the Mn containing catalysts (viz. Mn-Al, Mn-Fe, Mn-Cr hydroxides) do not show the presence of HT phase; these catalysts contain Mn-carbonate and Mn and other metal hydroxide phases. The Zn-Al-LDH, Cu-Cr-LDH, and Zn-Cr-LDH catalysts do not contain only HT phase but these have mixed HT and metal hydroxide/carbonate phases, as shown in Table 3.4. However the other LDH catalysts (viz. Co-Al-LDH, Ni-Al-LDH, Mg-Fe-LDH, Co-Fe-LDH, Ni-Fe-LDH, Co-Cr-LDH and Ni-Cr-LDH) have pure HT phase. The  $\text{CO}_2$  content is varied from catalyst to catalyst, depending upon the presence of HT phase and/or the transition elements present in the catalysts.

The  $\text{CO}_2$  content is very low in the Mn-Cr, Mn-Al, and Mn-Fe-hydroxides because of the absence of HT phase; consequently these catalysts do not have exchangeable  $\text{CO}_3^{2-}$  anions.

**Table 3.4:** Characterization of layered double hydroxide (LDH) catalysts containing different divalent [M(II)] and trivalent [M(III)] metals [M(II)/M(III) = 3.0].

M (II)	M (III)	XRD Phase(s)	d(001) spacing (nm)	CO <sub>3</sub> <sup>2-</sup> content (mmol.g <sup>-1</sup> )	pH of water slurry <sup>a</sup>	Surface area (m <sup>2</sup> .g <sup>-1</sup> )	t <sub>1/2</sub> <sup>b</sup> (min)
Mn	Al	Mn(OH) <sub>2</sub> , MnCO <sub>3</sub> , Al(OH) <sub>3</sub>	-	0.33	7.1	73	0.4
Co	Al	Pure HT	0.756	1.1	7.8	66	4.4
Ni	Al	Pure HT	0.784	1.07	8.0	119	7 % <sup>b</sup>
Zn,	Al	Pure HT, Zn(OH) <sub>2</sub> , Al(OH) <sub>3</sub>	0.751	0.71	7.5	46	n.d.
Mg	Fe	Pure HT	0.769	1.19	9.6	58	15.8
Mn	Fe	Mn(OH) <sub>2</sub> , MnCO <sub>3</sub> , Fe(OH) <sub>2</sub>	-	0.38	7.0	55	0.2
Co	Fe	Pure HT	0.760	0.57	7.4	75	0.8
Ni	Fe	Pure HT	0.775	0.66	7.0	60	22 % <sup>c</sup>
Zn	Fe	ZnCO <sub>3</sub> , FeCO <sub>3</sub> , Fe(OH) <sub>2</sub>	-	0.23	7.4	61	30 % <sup>c</sup>
Mg	Cr	Cr(OH) <sub>3</sub> .H <sub>2</sub> O, Mg(OH) <sub>2</sub>	-	1.14	9.9	107	15 % <sup>c</sup>
Mn	Cr	HT, Cr(OH) <sub>3</sub> .H <sub>2</sub> O, Mn(OH) <sub>2</sub> , MnCO <sub>3</sub>	0.748	0.09	6.3	96	0.9
Co	Cr	Pure HT	0.781	0.92	7.3	108	3.0
Ni	Cr	Pure HT	0.701	1.1	8.7	60	22 % <sup>c</sup>
Zn	Cr	HT, Zn(OH) <sub>2</sub> , ZnCO <sub>3</sub>	0.762	0.47	7.1	85	15 % <sup>c</sup>
Cu	Cr	HT, Cu(OH) <sub>2</sub> , CuCO <sub>3</sub>	0.748	0.98	7.4	111	9.7

<sup>a</sup>0.15 g catalyst in 10 ml distilled water, <sup>b</sup>t<sub>1/2</sub> = time for half H<sub>2</sub>O<sub>2</sub> decomposition. <sup>c</sup>Actual H<sub>2</sub>O<sub>2</sub> decomposition in 45 min [n.d. = not determined].

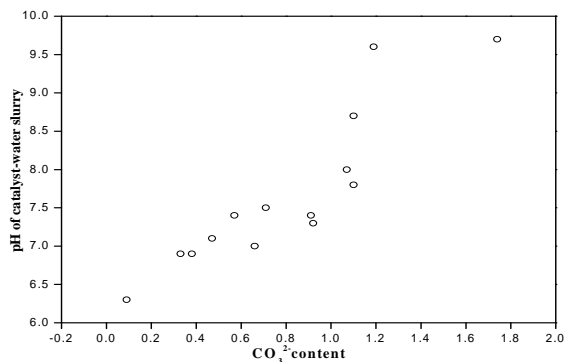


The basicity (measured in terms of the pH of catalyst-water slurry) of the Mn containing catalysts is very poor ( $\text{pH} \leq 7.0$ ). This is consistent with the fact that these catalysts do not contain HT phase. Earlier, Valente et al. [16] have found that the basicity of hydrotalcites is controlled by the electronegativity of their components and also changed by their chemical composition.

There is a large variation in the surface area of the catalysts, depending upon their composition. The surface area does not show any dependence on the presence or absence of HT phase in the catalysts.

The catalysts differ very widely in their  $\text{H}_2\text{O}_2$  decomposition activity (at 27 °C). The Mn containing catalysts have a very high  $\text{H}_2\text{O}_2$  decomposition activity (the  $t_{1/2}$  for the Mn-Al, Mn-Fe and Mn-Cr-hydroxides are 0.4, 0.2 and 0.9 min, respectively). The Co-Fe-LDH also has very high  $\text{H}_2\text{O}_2$  decomposition activity ( $t_{1/2} = 0.8$  min). The other catalysts except the Mg-Al-HT, Zn-Al-LDH, and Ni-Al-LDH catalysts show relatively a very poor  $\text{H}_2\text{O}_2$  decomposition activity. The other catalysts show intermediate to high activity for the  $\text{H}_2\text{O}_2$  decomposition.

A comparison of the  $\text{CO}_3^{2-}$  content and the pH data for the catalysts shows that there is a relationship between the two; Figure 3.4 shows that in general the pH (or the basicity) is increased with increasing the  $\text{CO}_3^{2-}$  content.



**Figure 3.4** Correlation between  $\text{CO}_3^{2-}$  content and the pH for various transition metals containing LDH catalysts

### 3.4.2 Activity of Layered Double Hydroxides (LDH) and Mixed Metal Hydroxides

Performance of Mn-Al, Co-Al, Ni-Al, Zn-Al, Mg-Fe, Mn-Fe, Co-Fe, Ni-Fe, Mn-Cr, Co-Cr, Ni-Cr, Cu-Cr, and Zn-Cr layered double hydroxides (LDH) solid catalysts have been evaluated for the liquid phase oxidation of benzyl alcohol to benzaldehyde using TBHP as an oxidizing agent in the absence of any solvent are presented in Table 3.5. It may be noted that the Mg-Al-HT showed little or no H<sub>2</sub>O<sub>2</sub> decomposition activity at 27 °C but very high H<sub>2</sub>O<sub>2</sub> decomposition activity at which the benzyl alcohol oxidation reaction is carried out. Hence, it is not possible to use H<sub>2</sub>O<sub>2</sub> as an oxidizing agent for the oxidation reaction over the catalysts used in the present studies.

The Mn-, Co- and Cu-containing LDH and Zn-Cr-LDH catalysts showed much higher benzyl alcohol conversion (41.9-59.5 %) than the pure Mg-Al-HT (20.2 %) and different Ni-containing LDH catalysts (15-17 %). Among the various bimetallic transition metal containing LDH catalysts, the best performance in terms of highest catalytic activity ( $\geq 52.5$  %) with good selectivity to benzaldehyde ( $\geq 70$  %) was observed over Co-containing LDH. It is interesting to note that the results achieved using Ni-containing catalysts are very close to the benzyl alcohol conversion (14.3 %) achieved in the absence of any catalyst. With the Zn-Al-LDH catalyst, the conversion was even less than that obtained in the absence of any catalyst indicating reaction inhibition due to the catalyst. A similar catalyst inhibition was also observed when the oxidation of benzyl alcohol by TBHP and molecular oxygen [8] was performed over Mg-Al-HT (Mg/Al = 10) and Ni containing hydrotalcite-like solid catalyst, respectively.

**Table 3.5:** Results of the liquid phase oxidation of benzyl alcohol to benzaldehyde over different layered double hydroxides (LDHs) [reaction conditions: reaction mixture = 52 mmol benzyl alcohol + 78 mmol TBHP + 0.5 g catalyst [M (II)/M (III) = 3.0], temperature = under reflux (bath temperature =  $94 \pm 1$  °C); reaction period = 5 h].

Catalyst	Conversion of Benzyl alcohol (%)	Selectivity (%)		
		Benzaldehyde	Benzoic acid	Benzyl benzoate
Mg-Al-HT	20.2	99.3	0.0	0.7
Mn-Al-LDH	46.7	91.3	7.7	0.97
Co-Al-LDH	56.7	77.4	17.5	5.0
Ni-Al-LDH	15.9	100	0.0	0.0
Zn-Al-LDH	10.5	100	0.0	0.0
Mg-Fe-LDH	19.4	97.7	0.1	2.2
Mn-Fe-LDH	53.9	70.6	27.5	1.9
Co-Fe-LDH	52.5	79.2	17.9	2.9
Ni-Fe-LDH	17.0	100	0.0	0.0
Mn-Cr-LDH	49.8	83.5	15.2	1.3
Co-Cr-LDH	59.5	70.0	24.0	6.0
Ni-Cr-LDH	15.0	100	0.0	0.0
Cu-Cr-LDH	51.3	74.9	6.6	18.5
Zn-Cr-LDH	41.9	91.5	6.5	2.0
Without catalyst	14.3	99.0	1.0	0.0

Bijlani and Chandalia [2] have reported very poor performance for Pd/C catalyst when the oxidation of benzyl alcohol by air was performed under solvent-free conditions. It is also reported earlier [5] that, in the presence of non-polar solvent (such as toluene) Ni-Al-hydrotalcite (Ni/Al = 2:1) shows an excellent performance in the oxidation by molecular oxygen of substituted benzyl alcohols to their corresponding aldehydes. However, in the present case, LDH-based catalysts showed both high activity and selectivity in the oxidation of benzyl alcohol in the absence of any solvent (Table 3.5). The solvent-free oxidation is practically very important to have environmentally more benign process.

Recently Farkas et. al. [17] have reported selective oxidation of benzylic alcohols to aldehydes using metallic nitrates as an oxidizing agent, over solid acid catalysts. In this case, although the aldehyde yields are higher than that obtained in the present case, the use of bismuth nitrates as an oxidizing agent in stoichiometric quantities and benzene as a solvent lead to production of undesirable waste.

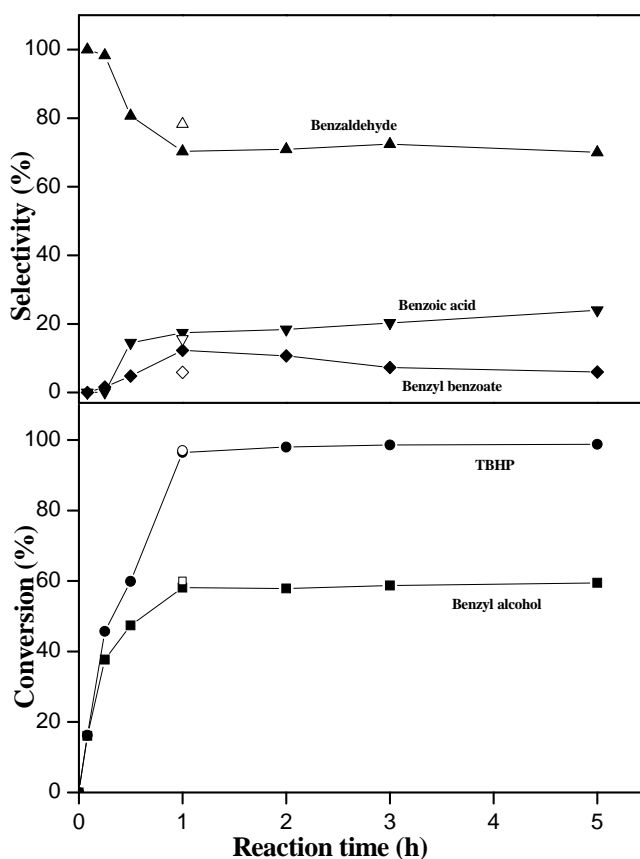
Among the transition metal (Table 3.5) containing layered double hydroxides (LDHs), the Mn-, Co- and Cu-containing LDH and the Zn-Cr-LDH are promising catalysts for the solvent-free liquid phase oxidation of benzyl alcohol to benzaldehyde. These catalysts could be reused without a significant loss in their activity and selectivity.

The influence of reaction time and temperature on the conversion and product selectivity in the benzyl alcohol oxidation by TBHP over Co-Cr-LDH, Co-Al-LDH and Mn-Fe-LDH are presented in Figures (3.5 - 3.9).

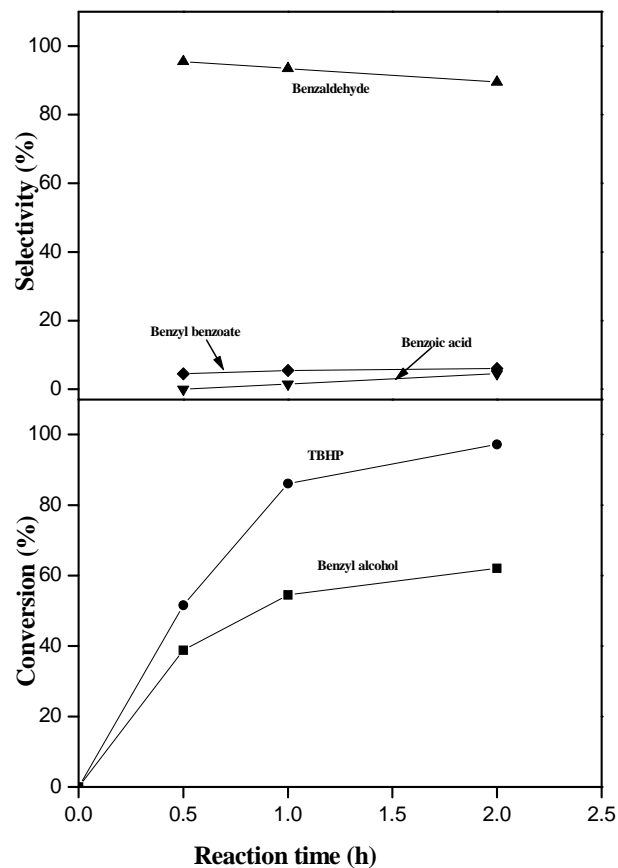
From the results (Figures 3.5 - 3.7), following general observations can be made about the influence of reaction temperature:

- At the lower temperature, the benzaldehyde selectivity is higher and the benzyl alcohol conversion is lower.

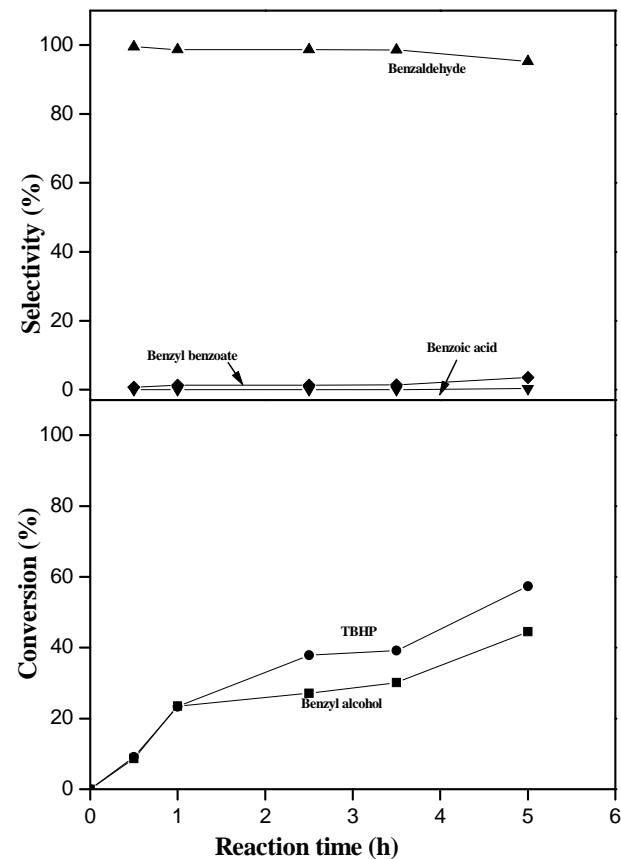
- As expected, with increasing the temperature the benzyl alcohol conversion increased markedly and the selectivity of benzaldehyde decreased and consequently the selectivity for benzyl benzoate increased significantly.



**Figure 3.5:** Variation with the reaction time of the conversion and product selectivity in the oxidation of benzyl alcohol over the Co-Cr-LDH (under reflux) [Hollow Symbols represents the results of reused catalyst].

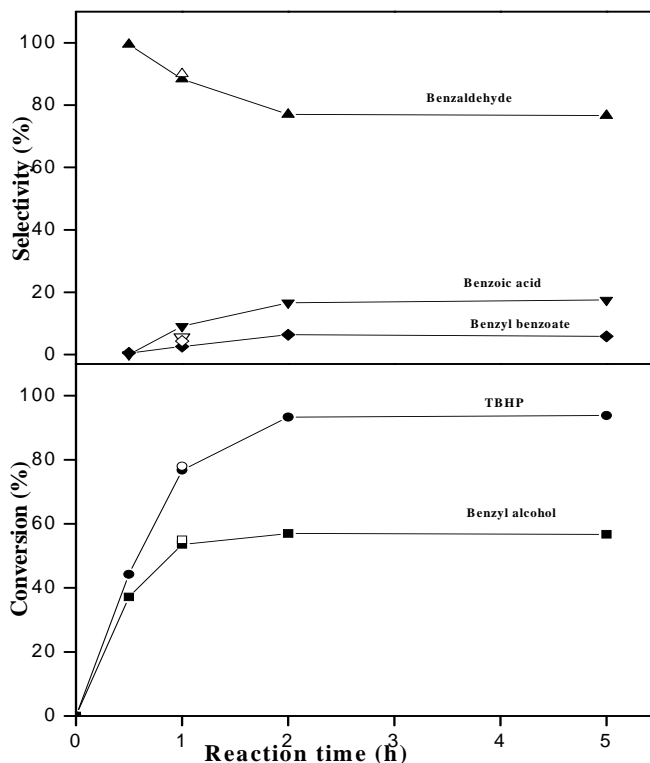


**Figure 3.6:** Variation with the reaction time of the conversion and product selectivity in the oxidation of benzyl alcohol over the Co-Cr-LDH (at 70 °C) [Hollow Symbols represents the results of reused catalyst]



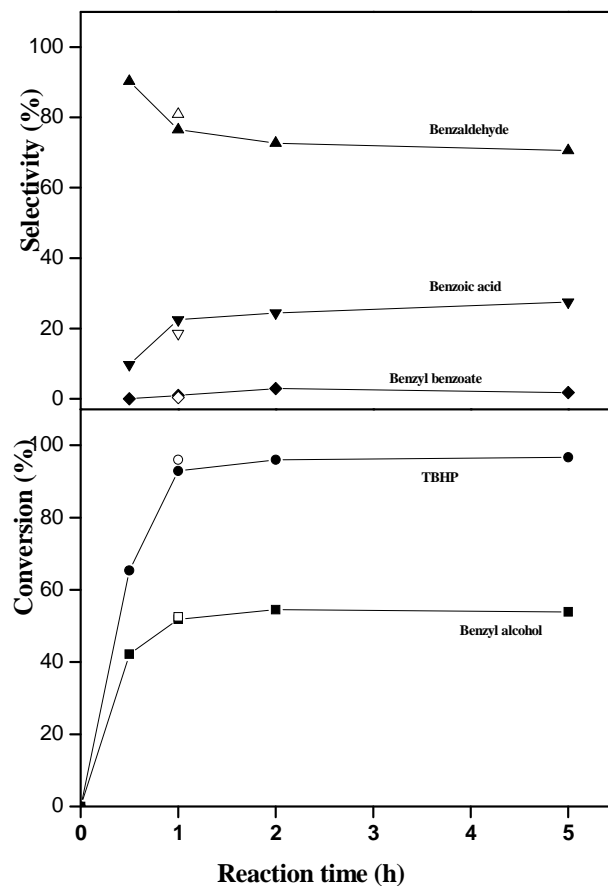
**Figure 3.7:** Variation with the reaction time of the conversion and product selectivity in the oxidation of benzyl alcohol over the Co-Cr-LDH (at 50 °C) [Hollow Symbols represents the results of reused catalyst]

Results showed the influence of reaction time on the conversion of benzyl alcohol and TBHP and product selectivity in the oxidation reaction over the catalysts (viz. Co-Cr-LDH, Co-Al-LDH, and Mn-Fe-LDH) showing good performance are presented in Figures 3.5 – 3.9.

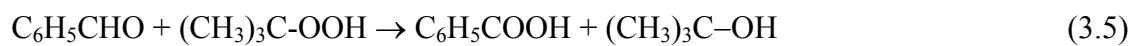


**Figure 3.8:** Dependence on the reaction time of the conversion and product selectivity in the oxidation of benzyl alcohol over the Co-Al-LDH (under reflux) [Hollow Symbols represents the results of reused catalyst].

With increasing the reaction time, the selectivity for benzaldehyde decreased while the conversion of both benzyl alcohol and selectivity for benzoic acid and benzyl benzoate increased. The consecutive reactions involved in the catalytic process are expected to be as follows:



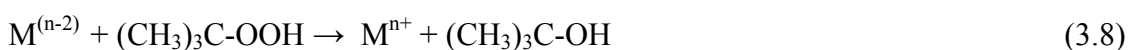
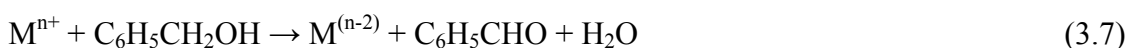
**Figure 3.9:** Dependence on the reaction time of the conversion and product selectivity in the oxidation of benzyl alcohol over the Mn-Fe-LDH (under reflux) [Hollow Symbols represents the results of reused catalyst].





The observed higher conversion of TBHP as compared to that of benzyl alcohol and the formation of benzoic acid in the reaction 3.5 is due to the catalytic decomposition of TBHP  $[(\text{CH}_3)_3\text{C-OOH} \rightarrow (\text{CH}_3)_3\text{C-OH} + 0.5 \text{O}_2]$ .

A comparison of the catalytic performance (Table 3.5 and Figures 3.4 - 3.9) with surface properties (Table 3.4) of the catalysts indicates that there is no direct relationship between their catalytic activity and selectivity in the oxidation and their surface area or basicity (measured in terms of the pH of water slurry). However, a direct correlation existed between the catalytic performance of the transition metal containing LDHs and/or HDs and their  $\text{H}_2\text{O}_2$  decomposition activity (Table 3.4); in general the catalysts showing high  $\text{H}_2\text{O}_2$  decomposition activity gave better performance in the selective oxidation of benzyl alcohol to benzaldehyde. The basic sites of the catalyst may be responsible for the activation of benzyl alcohol and/or TBHP. However, the oxidation of benzyl alcohol over the transition metal containing LDHs and/or MMHs catalysts is expected to involve a redox mechanism, similar to that described earlier [8], involving following two reactions:



Where, M = transition metal (e.g. Mn, Cr, Co, etc.) in the catalyst.

The Eq. (3.7) is expected to be the rate-controlling step in the oxidation.

The above results indicate that the catalyst is in general useful for the oxidation of benzylic alcohols to corresponding aldehydes with high selectivity/yield.

### 3.5 CONCLUSIONS

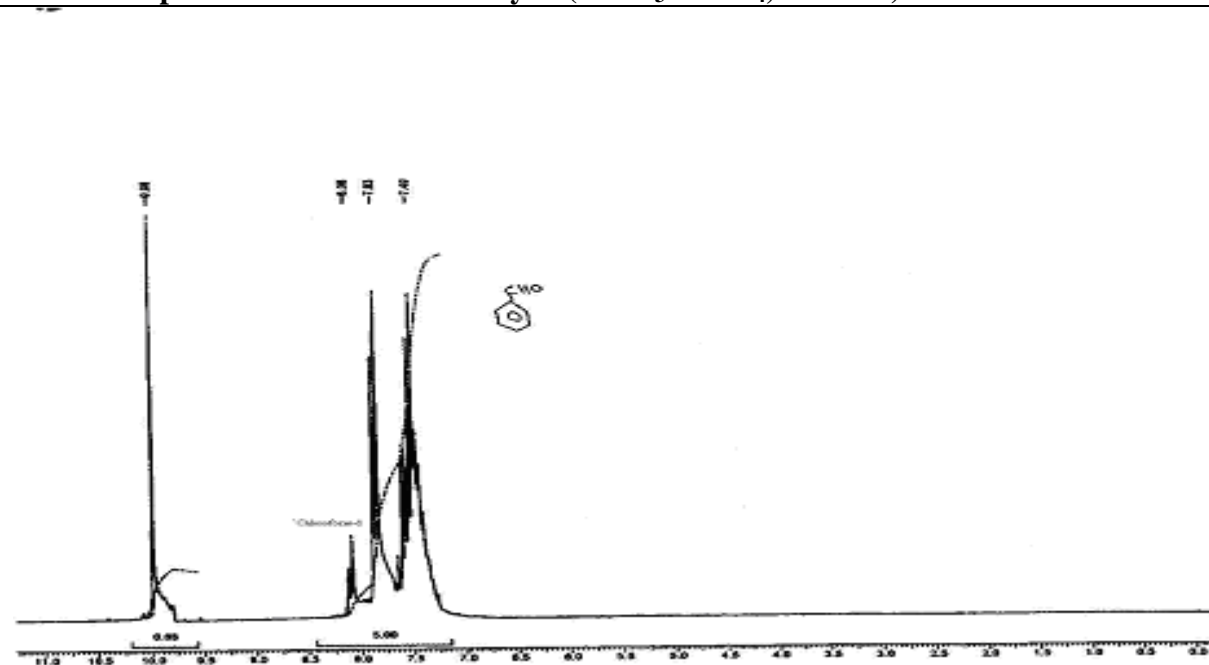
This investigations leads to following important conclusions:

- 1)  $\text{MnO}_4^-$ -exchanged Mg-Al-hydrotalcites (Mg/Al=2-10) show high activity and selectivity in the benzyl alcohol to benzaldehyde and benzaldehyde to benzoic acid oxidations by TBHP in the absence of any solvent.
- 2) The oxidation involves both the non-catalytic (homogeneous) and catalytic reactions. The catalytic reactions are confirmed to be heterogeneous one and its contribution to the oxidation is much higher than that of the homogeneous non-catalytic oxidation reaction.
- 3) Redox mechanism involving reduction of Mn(VII) to Mn(V) and oxidation of Mn(V) to Mn(VII) by TBHP seems to be operative in the catalytic oxidation process.
- 4) Among the transition metal (Co-Al, Ni-Al, Zn-Al, Mg-Fe, Mn-Fe, Co-Fe, Ni-Fe, Zn-Fe, Mg-Cr, Mn-Cr, Co-Cr, Ni-Cr, Zn-Cr and Cu-Cr) containing layered double hydroxides (LDHs) and /or mixed hydroxides, the Mn, Co and Cu and Zn-Cr containing LDH and/or mixed hydroxides are promising catalysts for the solvent-free liquid phase oxidation of benzyl alcohol to benzaldehyde. The Co containing LDH catalysts, however, show higher activity but lower benzaldehyde selectivity.

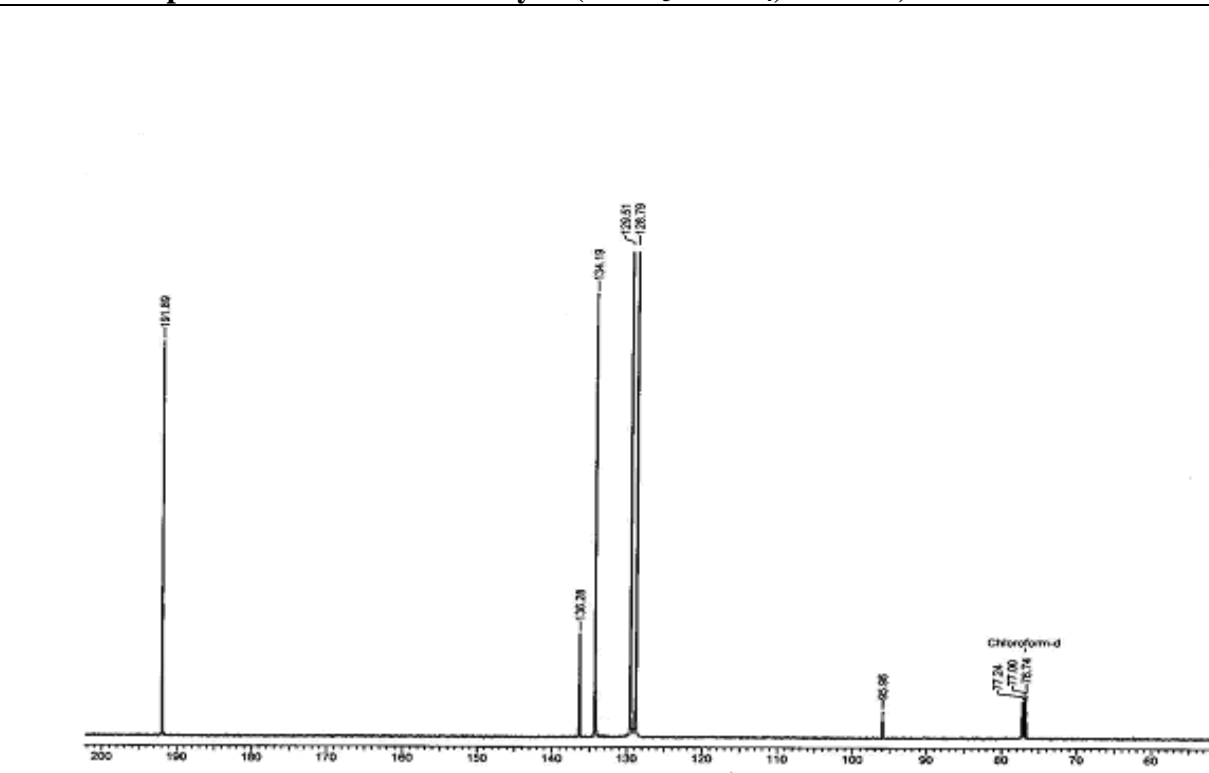
### Appendix-3.A

$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra of Oxidation reaction products

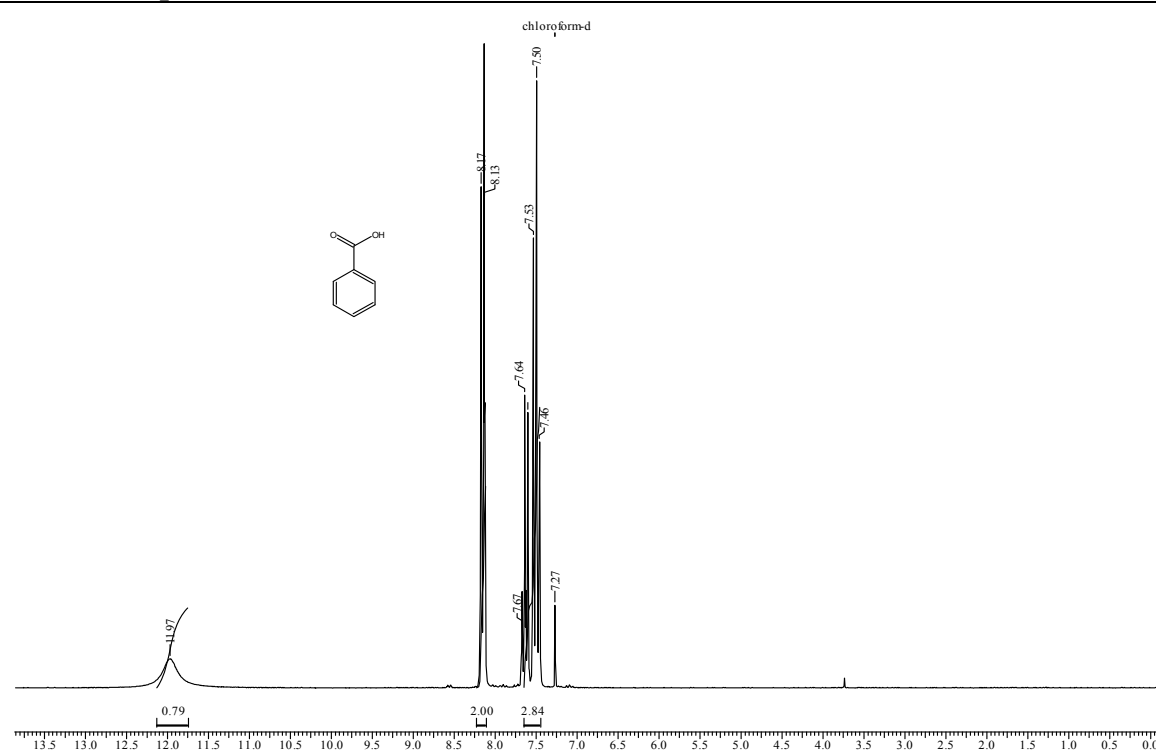
$^1\text{H}$  NMR Spectrum of the Benzaldehyde ( $\text{CDCl}_3 + \text{CCl}_4$ , 50 MHz)



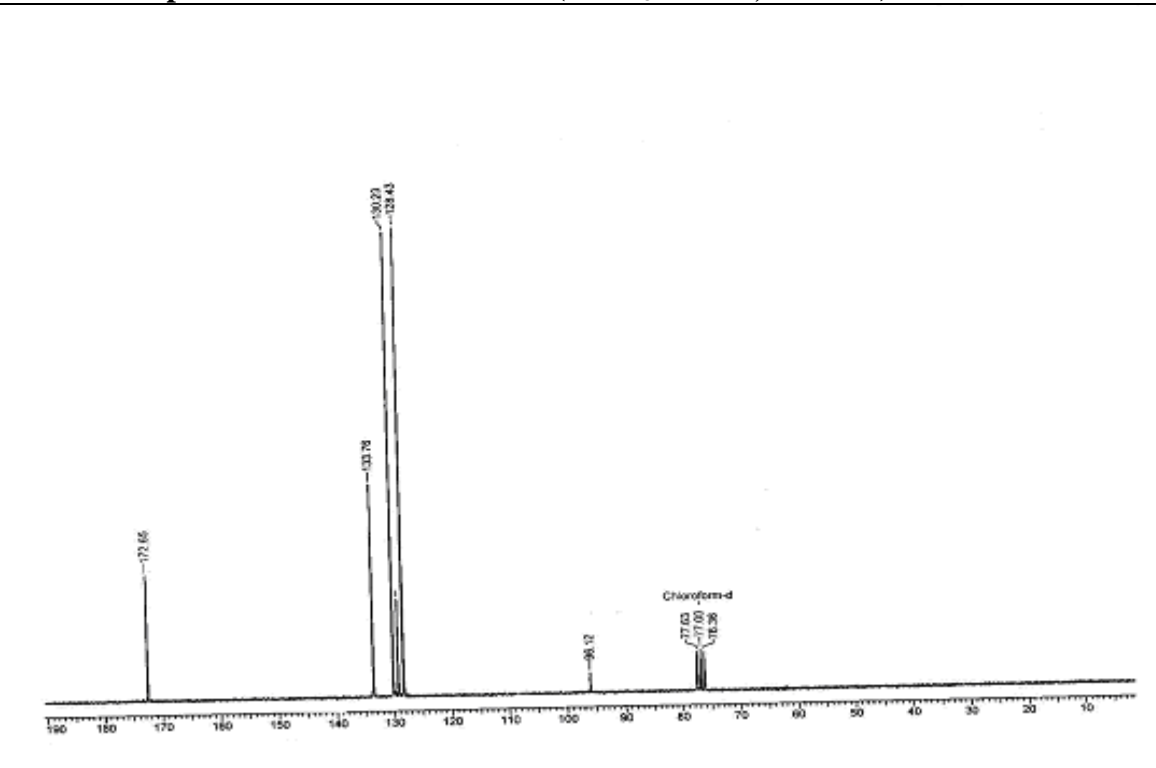
$^{13}\text{C}$  NMR Spectrum of the Benzaldehyde ( $\text{CDCl}_3 + \text{CCl}_4$ , 50 MHz)



**$^1\text{H}$  NMR Spectrum of the Benzoic acid ( $\text{CDCl}_3 + \text{CCl}_4$ , 50 MHz)**



**$^{13}\text{C}$  NMR Spectrum of the Benzoic acid ( $\text{CDCl}_3 + \text{CCl}_4$ , 50 MHz)**



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## **CHAPTER-4**

**Solvent-free Selective Oxidation of Benzyl  
Alcohol by TBHP to Benzaldehyde Using  
Supported Nano-gold Catalysts**

## CHAPTER-4

# Solvent-free Selective Oxidation of Benzyl Alcohol by TBHP to Benzaldehyde Using Supported Nano-gold Catalysts

### 4.1 BACKGROUND AND OBJECTIVE OF PRESENT WORK

Among the metals, the gold was believed to be inactive for its application as a catalyst. It has been shown that the low activity exhibited by the gold surface to absorb the molecules is because of the degree of orbital overlap and the filling of the antibonding states. Surface science investigation [1,2] and density function analysis [3] has also shown that no dissociative adsorption of H<sub>2</sub> and O<sub>2</sub> can take place over the smooth surfaces of Au at  $\leq 473$  K, indicating that Au should be catalytically inactive for oxidation and hydrogenation reactions. However, recently it has been found that the inertness of gold is broken when it is dispersed to nanometer scale especially on the metal oxide supports.

Haruta and coworkers [4,5] were the first to discover in 1987 that the particles of gold deposited on 3d transition metal oxides, prepared by co-preparation, are active for the CO oxidation at very low temperature, 200 K. This was a major breakthrough in the field of gold catalysis. In recent years, a dramatic growth of interest in the catalysis of nano-gold has occurred throughout the world. The most important discovery using gold catalysts is the vapor-phase epoxidation of propylene using H<sub>2</sub> and O<sub>2</sub> [6, 7]. After that, the high activity of gold supported on various metal oxides has been reported in a number of practically important reactions, such as NO decomposition [8,9], oxidation of CO [10,11], oxidation of hydrocarbons [12], epoxidation of propene [13] and selective hydrogenation [14,15].



Recently, Galvagno and coworkers [16,17] and Rossi and coworkers [18,19] have successfully used gold supported on  $\text{Fe}_2\text{O}_3$ ,  $\text{Co}_3\text{O}_4$ ,  $\text{NiO}$ ,  $\text{TiO}_2$  and  $\text{SiO}_2$  catalysts in the liquid-phase oxidation of benzylic alcohols to aldehydes or ketones. Few studies have been reported on the uranium oxide as a catalyst viz. oxidation of  $\text{CO}$  by  $\text{O}_2$  [20], oxidation of VOCs [21], catalytic reduction of  $\text{NO}_x$  [22], and oxidative destruction of short chain alkanes [23, 24]. Very recently, Choudhary and co-workers has reported different supported nano-gold catalysts as active and highly selective catalysts for the benzyl alcohol oxidation using molecular oxygen as an oxidant [25-26] and for the epoxidation of styrene to styrene oxide by TBHP [27].  $\text{U}_3\text{O}_8$  is also reported as an effective promoter for noble metals, viz.  $\text{Rh}$  and  $\text{Pt}$  in three-way catalysts in the presence of high sulfur levels [28].

It is, therefore, of both practical and scientific interest to explore the use of  $\text{Au}$  supported on different metal oxides (viz.  $\text{Fe}_2\text{O}_3$ ,  $\text{CuO}$ ,  $\text{CoO}$ ,  $\text{NiO}$ ,  $\text{MnO}_2$ ,  $\text{ZrO}_2$ ,  $\text{TiO}_2$ ,  $\text{ZnO}$ ,  $\text{MgO}$ ,  $\text{CaO}$ ,  $\text{BaO}$ ,  $\text{Al}_2\text{O}_3$ ,  $\text{Ga}_2\text{O}_3$ ,  $\text{In}_2\text{O}_3$ ,  $\text{La}_2\text{O}_3$ ,  $\text{Sm}_2\text{O}_3$ ,  $\text{U}_3\text{O}_8$ ,  $\text{Yb}_2\text{O}_3$  and  $\text{Eu}_2\text{O}_3$ ), as reusable highly active solid catalysts, for the selective oxidation of benzyl alcohol to benzaldehyde by anhydrous TBHP, under solvent-free conditions, to make the processes environmentally more benign. The present work was undertaken with the following objectives:

1. To prepare, characterize and evaluate for the benzyl alcohol to benzaldehyde oxidation of a number of different supported nano-gold catalysts, such as

- nano-gold supported on different alkaline earth oxides,
- nano-gold supported on different Gr.IIIA metal oxides,
- nano-gold supported on different transition metal oxides and
- nano-gold supported on different rare earth oxides,

all prepared by the homogeneous deposition precipitation (HDP) method.

2. To investigate in details the oxidation reaction over a selected few catalysts (viz. Au/TiO<sub>2</sub>, Au/MgO and Au/U<sub>3</sub>O<sub>8</sub>).

Influence of Au loading in these catalysts, method of Au loading, catalyst calcination temperature and reaction conditions on the catalyst performance in the benzyl alcohol to benzaldehyde oxidation has also been studied.

#### **4.2 CATALYSTS AND BRIEF EXPERIMENTAL PROCEDURE**

A number of different supported nano-gold catalysts were prepared. Gold was deposited on the alkaline earth oxides, Gr. IIIA metal oxides, transition metal oxides and rare earth oxides were prepared by the four different methods (DP, HDP, co-precipitation and impregnation) as described earlier [Chapter 2, section 2.2.3].

The catalysts were characterized for their crystalline phase(s) by XRD [using a Phillips Diffractometer (1730 series) and CuK $\alpha$  radiations], for their surface area by the single point N<sub>2</sub> adsorption method (using a Surface Area Analyser; Quanta Chrome, USA), ICP-OES (using Perkin Elmer Analyzer), TEM analysis was done using a JEOL (Model No. JEM 1200 EX) and XPS [using a VG-Scientific ESCA-3 MK-II electron spectrometer (C1s with binding energy = 285.0 eV) was used as internal standard].

The catalytic oxidation of benzyl alcohol was carried out in a magnetically stirred round bottom flask (capacity: 25 cm<sup>3</sup>), provided with a mercury thermometer for measuring the reaction temperature and reflux condenser as already shown in Figure 2.1 (Chapter 2), at the following reaction conditions: reaction mixture = 52 mmol benzyl alcohol + 78 mmol TBHP (70 % TBHP in water) + 0.5 g catalyst, temperature = 92-95 °C (under reflux at a bath temperature of 97 °C), reaction time = 5 h. The reaction products were analyzed by gas chromatograph with flame ionization detector, using a SE-30 column and N<sub>2</sub> as a carrier gas.

### 4.3 PERFORMANCE OF SUPPORTED NANO-GOLD CATALYSTS

The results showing nano-gold supported on alkaline earth metal oxides (MgO, CaO, SrO and BaO) and Gr. IIIA metal oxides ( $\text{Al}_2\text{O}_3$ ,  $\text{Ga}_2\text{O}_3$  and  $\text{In}_2\text{O}_3$ ) catalysts on oxidation of benzyl alcohol by TBHP, prepared by HDP method are presented in Table 4.1.

**Table 4.1:** Performance of the nano-gold supported on alkaline earth metal oxides and Gr. IIIA metal oxides in the oxidation of benzyl alcohol to benzaldehyde by TBHP in absence of any solvent [reaction conditions: = 52 mmol benzyl alcohol + 78 mmol TBHP (70 % TBHP in water) + 0.5 g catalyst, temperature under reflux (bath temperature of 92-95 °C), reaction time = 2 h].

Catalyst	Au loading (wt %)	Surface area ( $\text{m}^2/\text{g}$ )	Au particle size (nm)	Conversion of benzyl alcohol (%)	Selectivity (%)	
					BZH <sup>a</sup>	BB <sup>b</sup>
Au/MgO	7.5	47.2	8.4	99.8	69.5	30.4
Au/CaO	4.7	3.3	9.3	40.8	85.9	14.0
Au/SrO	5.0	7.5	9.7	45.7	83.5	16.4
Au/ BaO	5.3	10.4	6.6	53.2	80.5	19.4
Au/ $\text{Al}_2\text{O}_3$	6.4	147.0	4.8	70.5	65.2	34.7
Au/ $\text{Ga}_2\text{O}_3$	6.5	17.4	6.1	55.8	78.2	21.7
Au/ $\text{In}_2\text{O}_3$	6.8	3.5	14.7	56.7	74.7	25.2

<sup>a</sup>BZH = Benzaldehyde, <sup>b</sup>BB = Benzyl benzoate

The results showing the performance of nano-gold supported on different transition metal oxides and rare earth oxides catalysts, prepared by HDP method, in the oxidation of benzyl alcohol by TBHP are presented in Table 4.2.

Although the same amount of gold was available for the different metal oxides for gold deposition by the HDP method, the gold loading varies from catalyst to catalyst, depending upon the metal oxide (support) used in the catalyst.

The acid-base properties of the metal oxide supports were evaluated in terms of the pH of the metal oxide-water slurry (0.1 g finely ground metal oxide in 10 ml deionized water). No direct correlation between the gold loading and the support surface properties is observed (Tables 4.1 and 4.2). The gold particle size shows a decreasing trend with increasing the surface area (Tables 4.1 and 4.2). This is expected because of a better dispersion of gold on the support having larger surface area.

From the results (Tables 4.1 and 4.2), following important observations have been made:

- Among the alkaline earth and Gr. III metal oxide supported gold catalysts, the Au/MgO catalyst showed the best performance [both high activity (99.8 % conversion of benzyl alcohol) and selectivity (69.5 % for benzaldehyde)] (Table 4.1).
- Among the supported gold catalysts, the transition metal oxide, the Au/TiO<sub>2</sub> catalyst showed the best performance with good conversion (63.1%) and selectivity (79.2 %), (Table 4.2).
- Among the supported gold catalysts, the rare earth oxide, the Au/U<sub>3</sub>O<sub>8</sub> catalyst showed the best performance (99.9 % conversion with 73.5 % selectivity for benzaldehyde), (Table 4.2).
- The other supported gold catalysts, particularly Au/Al<sub>2</sub>O<sub>3</sub>, Au/SrO, Au/Ga<sub>2</sub>O<sub>3</sub>, Au/Fe<sub>2</sub>O<sub>3</sub>, Au/MnO<sub>2</sub>, Au/CoO and Au/ZrO<sub>2</sub> also showed good activity in the benzyl alcohol to benzaldehyde oxidation.

**Table 4.2:** Performance of the nano-gold supported on transition metal oxides and rare earth oxides in the oxidation of benzyl alcohol to benzaldehyde by TBHP in absence of any solvent [reaction conditions: = 52 mmol benzyl alcohol + 78 mmol TBHP + 0.5 g catalyst, temperature = 92-95 °C), reaction time = 2 h].

Catalyst	Au loading (wt %)	Surface area (m <sup>2</sup> /g)	Au particle size (nm)	Conversion of benzyl alcohol (%)	Selectivity (%)	
					BZH <sup>a</sup>	BB <sup>b</sup>
Au/TiO <sub>2</sub>	6.0	3.5	4.9 ± 0.5	63.1	79.2	20.7
Au/MnO <sub>2</sub>	4.2	14.3	5.7 ± 1.7	54.6	73.2	26.7
Au/Fe <sub>2</sub> O <sub>3</sub>	6.1	12.4	6.1 ± 0.3	29.6	88.7	11.2
Au/CoO	7.1	23.8	5.0 ± 1.3	34.0	85.2	14.7
Au/NiO	6.2	4.0	19.5 ± 3.2	37.5	82.5	17.4
Au/CuO	6.8	3.3	10.9 ± 2.6	39.0	75.5	24.4
Au/ZnO	6.6	6.1	4.1 ± 0.5	45.0	71.2	18.7
Au/ ZrO <sub>2</sub>	3.3	36.5	4.5 ± 1.2	59.5	81.5	18.5
Au/La <sub>2</sub> O <sub>3</sub>	6.5	5.9	8.5 ± 0.5	55.2	70.1	29.8
Au/Sm <sub>2</sub> O <sub>3</sub>	4.2	3.2	7.1 ± 0.5	50.4	63.2	36.7
Au/ Eu <sub>2</sub> O <sub>3</sub>	6.6	5.7	9.5 ± 0.5	45.5	75.3	24.6
Au/Yb <sub>2</sub> O <sub>3</sub>	6.6	2.7	10.1 ± 0.5	47.5	80.6	19.3
Au/U <sub>3</sub> O <sub>8</sub>	8.0	6.5	9.4 ± 0.5	99.9	73.5	26.4

<sup>a</sup>BZH = Benzaldehyde, <sup>b</sup>BB = Benzyl benzoate

The TEM photographs of the nano-gold particles supported on alkaline earth metal oxides and Gr. IIIA metal oxides (prepared by the HDP method) are presented in Figure 4.1.

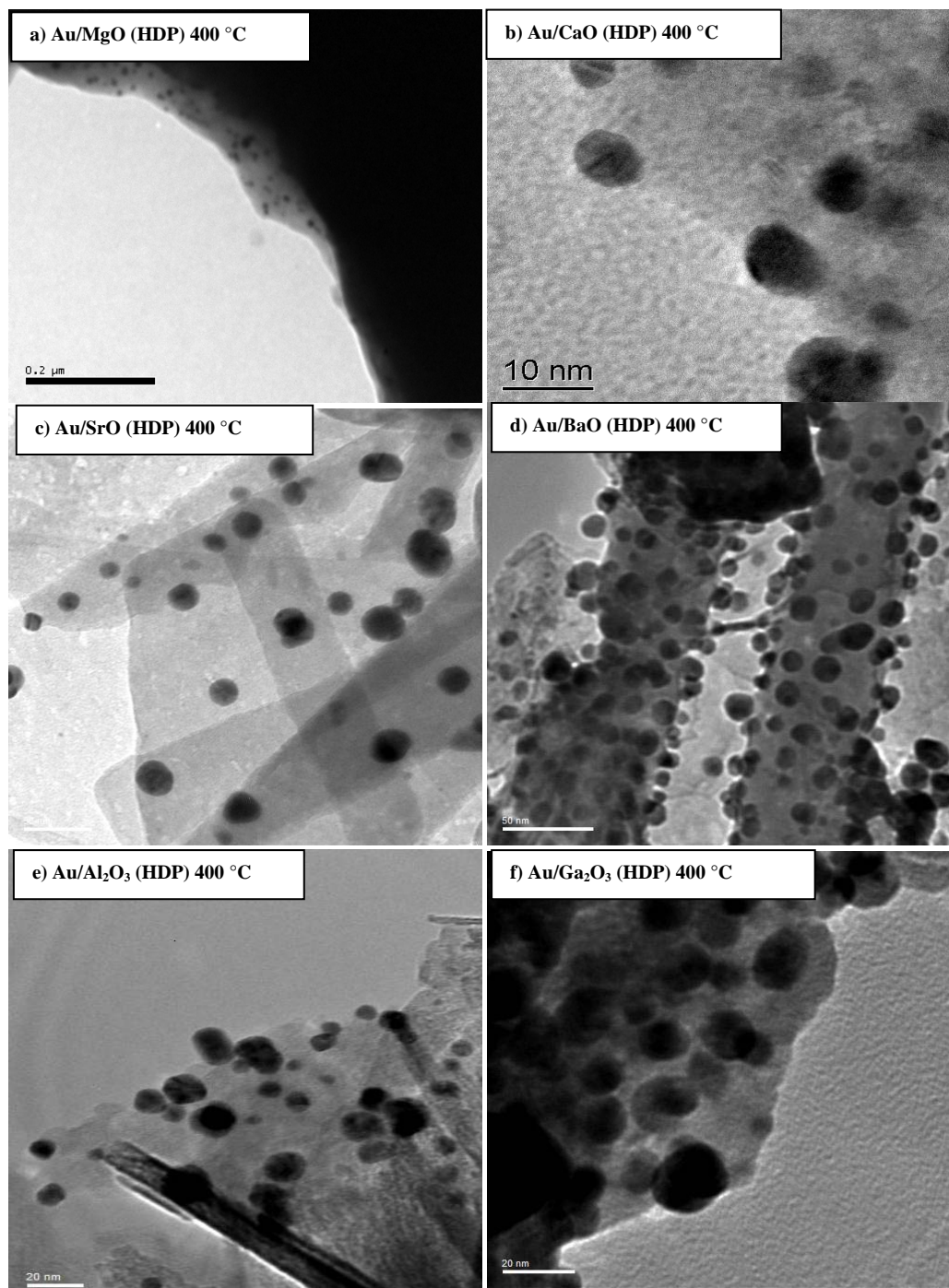
The TEM photographs of nano-gold supported on transition metal oxides and rare earth metal oxides (prepared by the HDP method) are presented in Figures 4.2 and 4.3.

A comparison of the results in Tables 4.1 and 4.2 reveal a strong influence of metal oxide support on the catalytic performance of the supported gold catalysts (both the benzyl alcohol conversion activity and product selectivity in the oxidation of benzyl alcohol to benzaldehyde are influenced). However, it may be noted that the supported gold catalysts do not have the same gold loading. The amount of gold deposited on the support by the HDP is strongly influenced by the metal oxide support (the gold available for the deposition on all the support was the same).

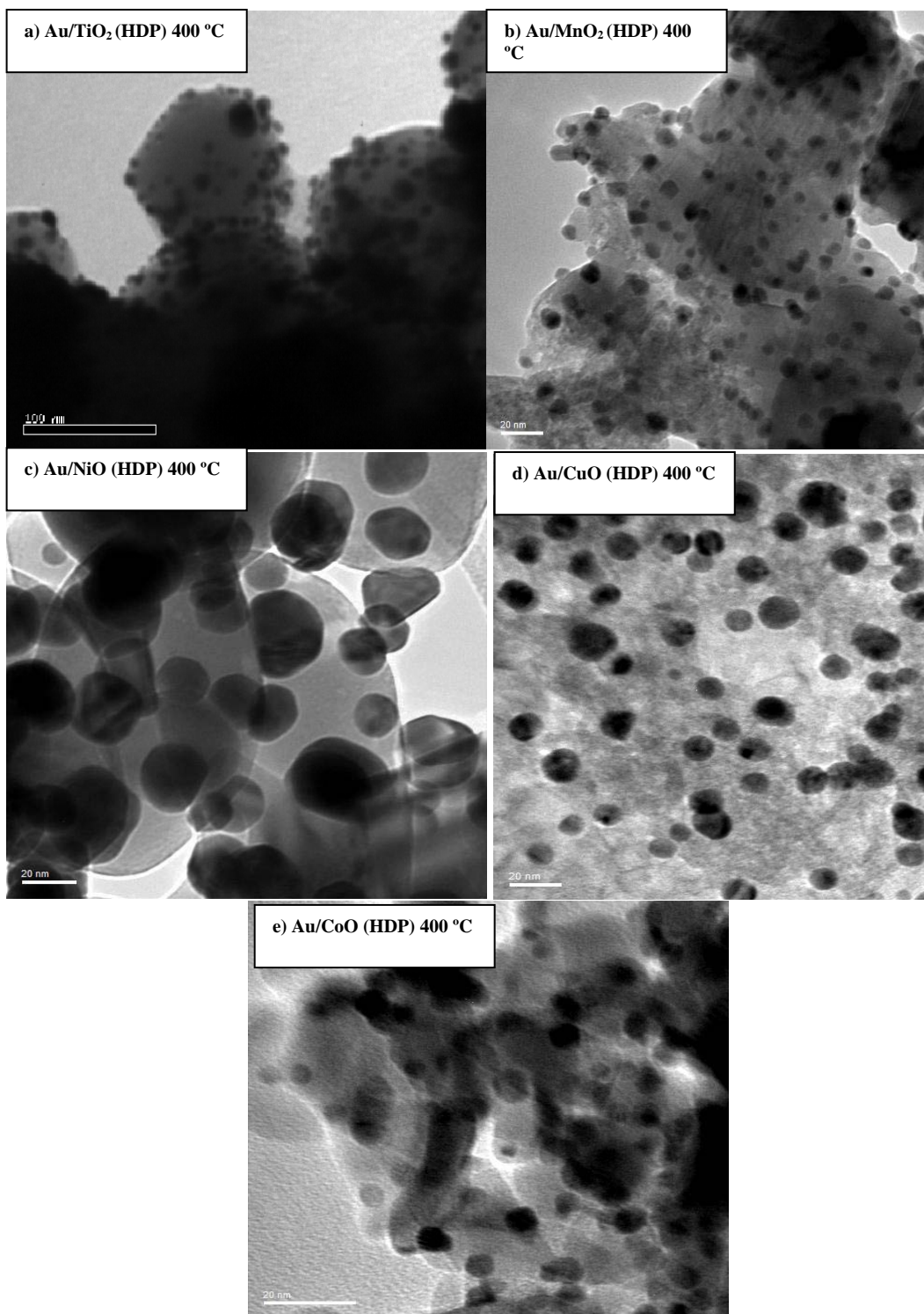
It is, however, interesting to note that, inspite of the lowest Au loading, the Au/ZrO<sub>2</sub> catalyst shows good catalytic activity. This may be because of the lower Au particle size of the Au/ZrO<sub>2</sub>. A comparison of the data in Tables 4.1 and 4.2 also indicates that there is no direct relationship between the Au loading and the catalytic performance in the benzyl alcohol oxidation. This may be mostly because of the fact that the au particle size varies from catalyst to catalyst.

From the comparisons based on the benzaldehyde yield, the following general observation can however be made:

- The gold supported on the reducible metal oxides (e.g. NiO, CuO, CoO, Fe<sub>2</sub>O<sub>3</sub> and ZnO), shows poor activity in the benzyl alcohol to benzaldehyde oxidation.
- The gold catalysts supported on some non-reducible or difficult to reduce metal oxides (e.g. ZrO<sub>2</sub>, Al<sub>2</sub>O<sub>3</sub>, U<sub>3</sub>O<sub>8</sub>, MgO, CaO, BaO, La<sub>2</sub>O<sub>3</sub>, Sm<sub>2</sub>O<sub>3</sub>, Eu<sub>2</sub>O<sub>3</sub>, Yb<sub>2</sub>O<sub>3</sub>, etc.) shows a good performance in the oxidation.

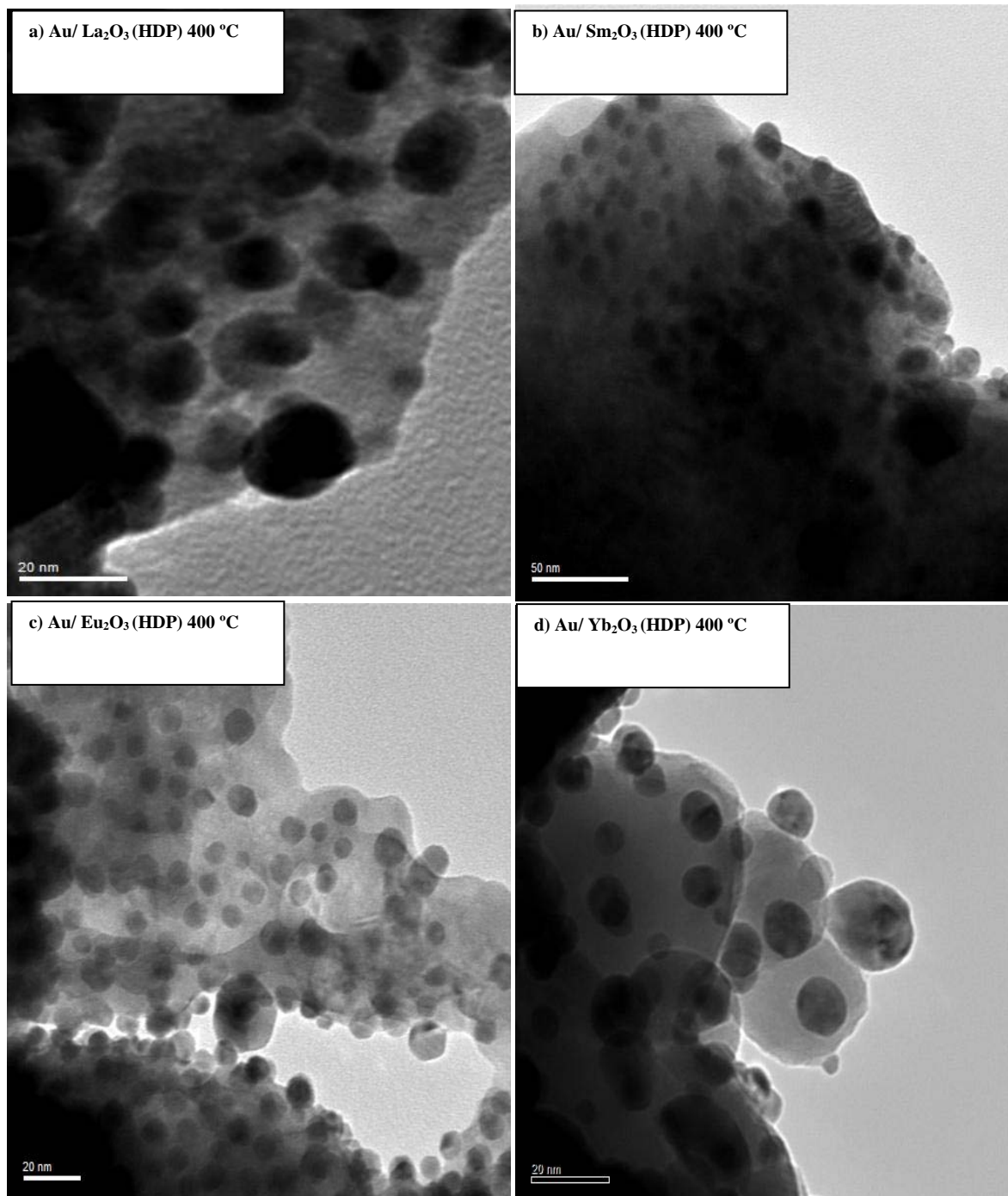


**Figure 4.1:** TEM photographs of a) Au/MgO (HDP) 400 °C, b) Au/CaO (HDP) 400 °C, c) Au/SrO(HDP) 400 °C, d) Au/BaO(HDP) 400 °C, e) Au/Al<sub>2</sub>O<sub>3</sub>(HDP) 400 °C, f) Au/Ga<sub>2</sub>O<sub>3</sub> (HDP) 400 °C,



**Figure 4.2:** TEM photographs of a) Au/ TiO<sub>2</sub> (HDP)400 °C, b) Au/ MnO<sub>2</sub>(HDP) 400 °C, c)Au/ NiO (HDP) 400 °C, d)Au/ CuO(HDP)400 °C, e)Au/CoO(HDP) 400 °C.





**Figure 4.3:** TEM photographs of a) Au/ La<sub>2</sub>O<sub>3</sub> (HDP) 400 °C, b) Au/ Sm<sub>2</sub>O<sub>3</sub> (HDP) 400 °C, c) Au/ Eu<sub>2</sub>O<sub>3</sub> (HDP) 400 °C, d) Au/ Yb<sub>2</sub>O<sub>3</sub> (HDP) 400 °C.

The interaction between the supported gold and the support seems to play an important role in deciding both the gold particle size and catalytic performance of the supported gold catalysts. Further detailed studies are essential for understanding the important role played by the support for controlling the deposition of gold (i.e. gold loading), gold particle size and catalytic performance of supported gold catalysts.

From the product distributions, following consecutive reactions are expected to occur in the benzyl alcohol oxidation by TBHP:



It is interesting to note that the absence of benzoic acid in the GC and GC-MS analysis indicates that, as soon as benzoic acid is formed, it reacts immediately with benzyl alcohol, which is available in much higher concentration, forming benzyl benzoate.

#### **4.4 OXIDATION OF BENZYL ALCOHOL OVER Au/TiO<sub>2</sub> CATALYST**

Since the Au/TiO<sub>2</sub> catalyst showed highly promising performance in the benzyl alcohol to benzaldehyde oxidation, from the transition metal oxides group, it was interesting to carry out further detailed investigation on this catalyst. Influence of various Au deposition methods for the preparation of Au/TiO<sub>2</sub> and Au loading in the catalyst (prepared by DP and HDP methods) on the surface properties and performance of the catalyst in the benzyl alcohol to benzaldehyde oxidation has been investigated.

##### **4.4.1 Influence of Au Deposition Method on Surface Properties**

The results showing the influence of gold loading (measured by ICP-OES), surface area and Au particle size (measured by TEM and/or XRD) of the Au/TiO<sub>2</sub> catalyst, prepared by the

DP and HDP methods are presented in Table 4.3. As compared to the DP method, the HDP method provided much higher gold loading on the TiO<sub>2</sub> support. The results are consistent with those observed earlier by Zanella et al. [29]. The observed large difference in the gold loadings for the Au/TiO<sub>2</sub> catalysts prepared by the DP and HDP methods is attributed to the large difference in the pH of the solution containing gold in the two cases, as explained earlier [27,29].

**Table 4.3:** Properties of Au/TiO<sub>2</sub> catalysts, prepared by DP and HDP methods.

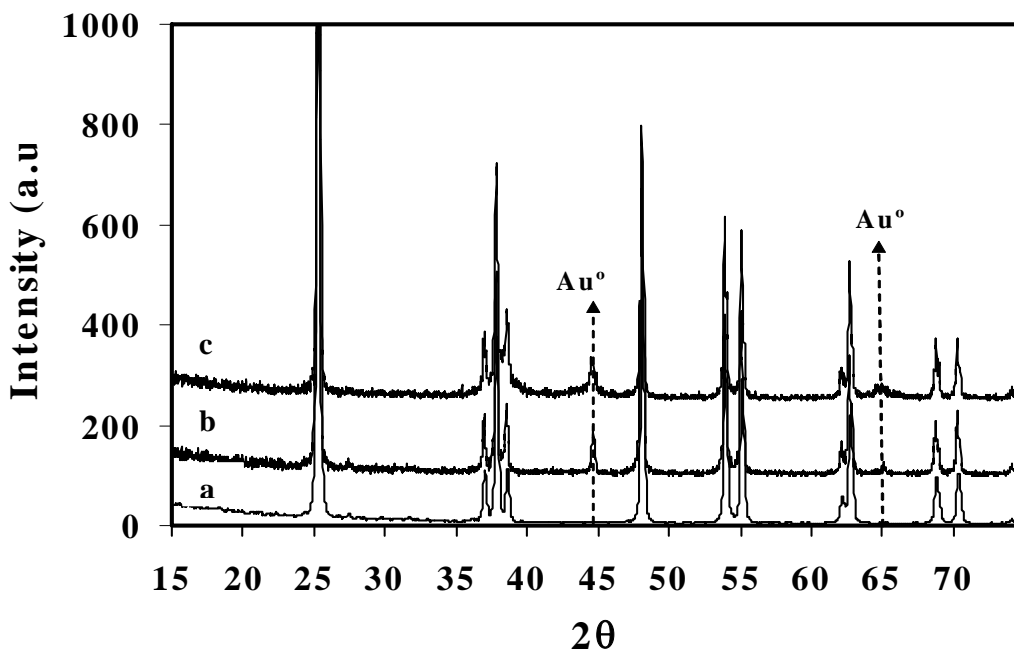
Au (mmol. g <sup>-1</sup> )		Surface area (m <sup>2</sup> .g <sup>-1</sup> )	Au particle size (nm)	Surface Au <sup>+3</sup> /Au <sup>0</sup> ratio
Present in the solution	Deposited on the TiO <sub>2</sub>			
<b><i>a) Au/TiO<sub>2</sub> prepared by the DP method</i></b>				
0.05	0.001	15.9	-	-
0.10	0.004	9.0	-	-
0.20	0.013	8.8	-	-
0.40	0.024	8.0	11.7 ± 0.5 (12.1) <sup>a</sup>	0.06
<b><i>b) Au/TiO<sub>2</sub> prepared by the HDP method</i></b>				
0.05	0.04	9.6	-	-
0.10	0.09	9.1	-	-
0.20	0.17	8.0	-	-
0.40	0.30	3.4	4.9 ± 0.5 (5.7) <sup>a</sup>	0.18

<sup>a</sup> Measured by XRD for Au (200) peak ( $2\theta = 44.38^\circ$ ).

It is interesting to note that the surface area of TiO<sub>2</sub> support (19 m<sup>2</sup>. g<sup>-1</sup>) is decreased appreciably with increasing the Au loading on the support for Au/TiO<sub>2</sub> prepared by both the DP and HDP methods (Table 4.3).

The XRD spectra of the TiO<sub>2</sub> and Au/TiO<sub>2</sub>(DP) and Au/TiO<sub>2</sub>(HDP) are presented in Figure 4.4. The XRD spectra of the TiO<sub>2</sub> (XRD major peak at  $2\theta = 25.3$ ) indicate the presence

of pure anatase phase. The XRD spectra of both the Au/TiO<sub>2</sub> (DP and HDP) catalysts also show the presence of pure anatase phase for TiO<sub>2</sub> and gold in the metallic (Au<sup>0</sup>) form. The particle size observed from XRD spectra was (5.7 nm) and (12.1nm) for the Au/TiO<sub>2</sub>(HDP) and Au/TiO<sub>2</sub>(DP), respectively.

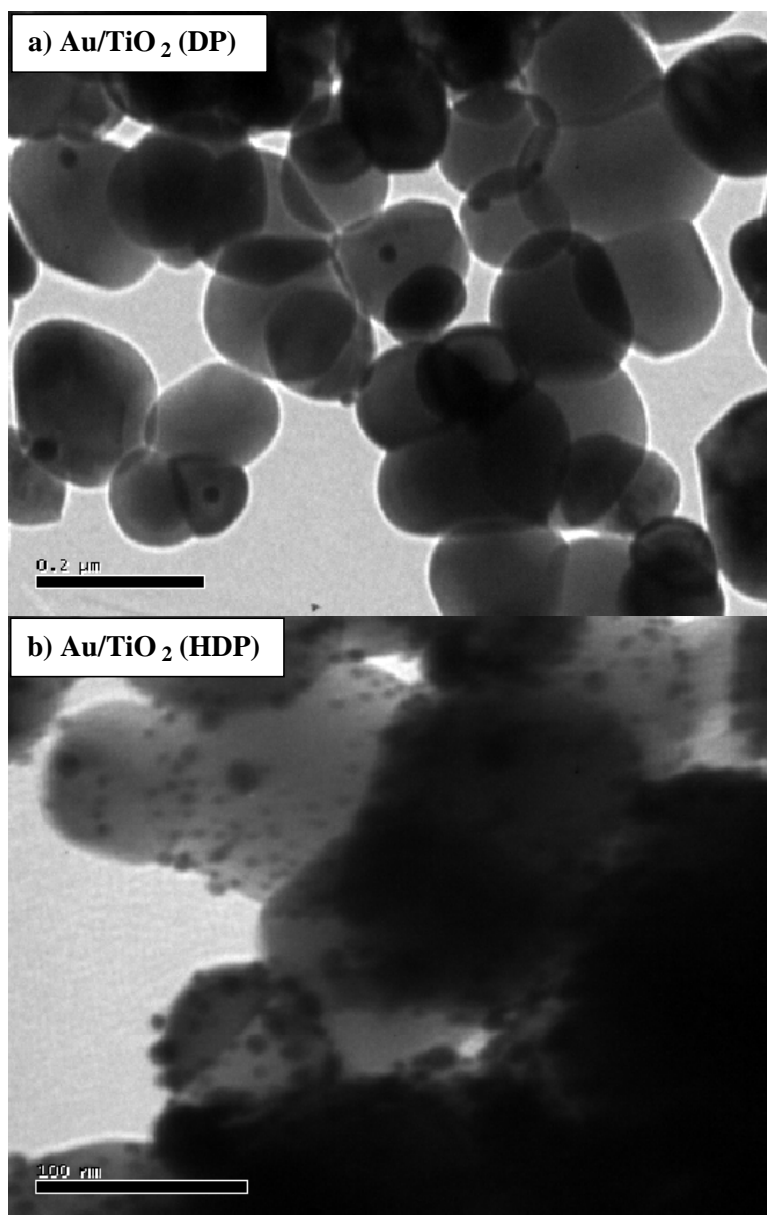


**Figure 4.4:** XRD of TiO<sub>2</sub>, and Au supported TiO<sub>2</sub>, a) TiO<sub>2</sub>, b) Au/TiO<sub>2</sub> (DP) and c) Au/TiO<sub>2</sub> (HDP) catalysts.

The TEM photographs of Au/TiO<sub>2</sub> catalysts prepared by the DP and HDP methods are presented in Figure 4.5.

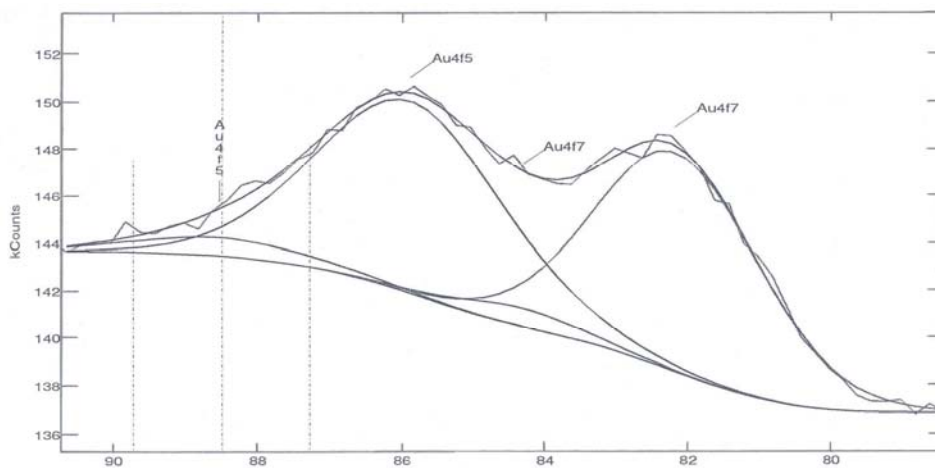
It may be noted that the TEM pictures shown in Figure 4.5 are representative one. The catalyst prepared by the HDP method shows the presence of homogeneously dispersed smaller gold particles ( $4.9 \pm 0.5$  nm) as compared to that observed for the Au/TiO<sub>2</sub> catalyst prepared by the DP method ( $11.7 \pm 0.5$  nm). The concentration of Au particles for the Au/TiO<sub>2</sub> (DP) is also found to be much smaller. The TEM picture in Figure 4.5b shows that the Au on the TiO<sub>2</sub>

support is in the form of hemispherical particles strongly interacting with the support, similar to that observed earlier [30].

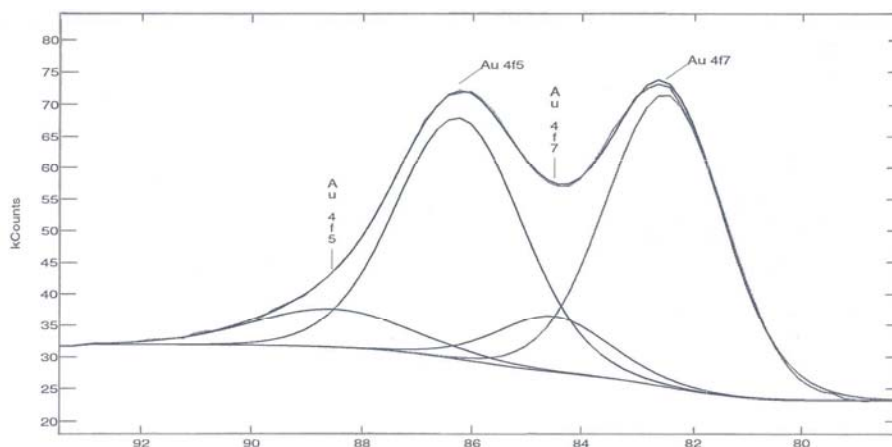


**Figure 4.5:** TEM of Au/TiO<sub>2</sub> (DP) and Au/TiO<sub>2</sub> (HDP) catalysts

The XPS spectrum of the Au/TiO<sub>2</sub> (DP) catalyst (Figure 4.6) shows that the binding energy values for Au4f<sub>5</sub> are 89.04 and 86.38 eV, and that for Au4f<sub>7</sub> are 84.82 and 82.68 eV. Whereas, for the Au/TiO<sub>2</sub> (HDP) catalyst, the binding energy values are found to be 85.01 and 83.0 eV for Au4f<sub>7</sub>, and 89.05 and 86.75 eV for Au4f<sub>5</sub> (Figure 4.7).



**Figure 4.6:** XPS Spectra of Au4f electrons of Au (0.024 mmol g<sup>-1</sup>)/TiO<sub>2</sub> (DP) catalyst calcined at 400 °C for 2 h.



**Figure 4.7:** XPS Spectra of Au4f electrons of Au (0.3 mmol g<sup>-1</sup>)/TiO<sub>2</sub> (HDP) catalyst calcined at 400 °C for 2 h.

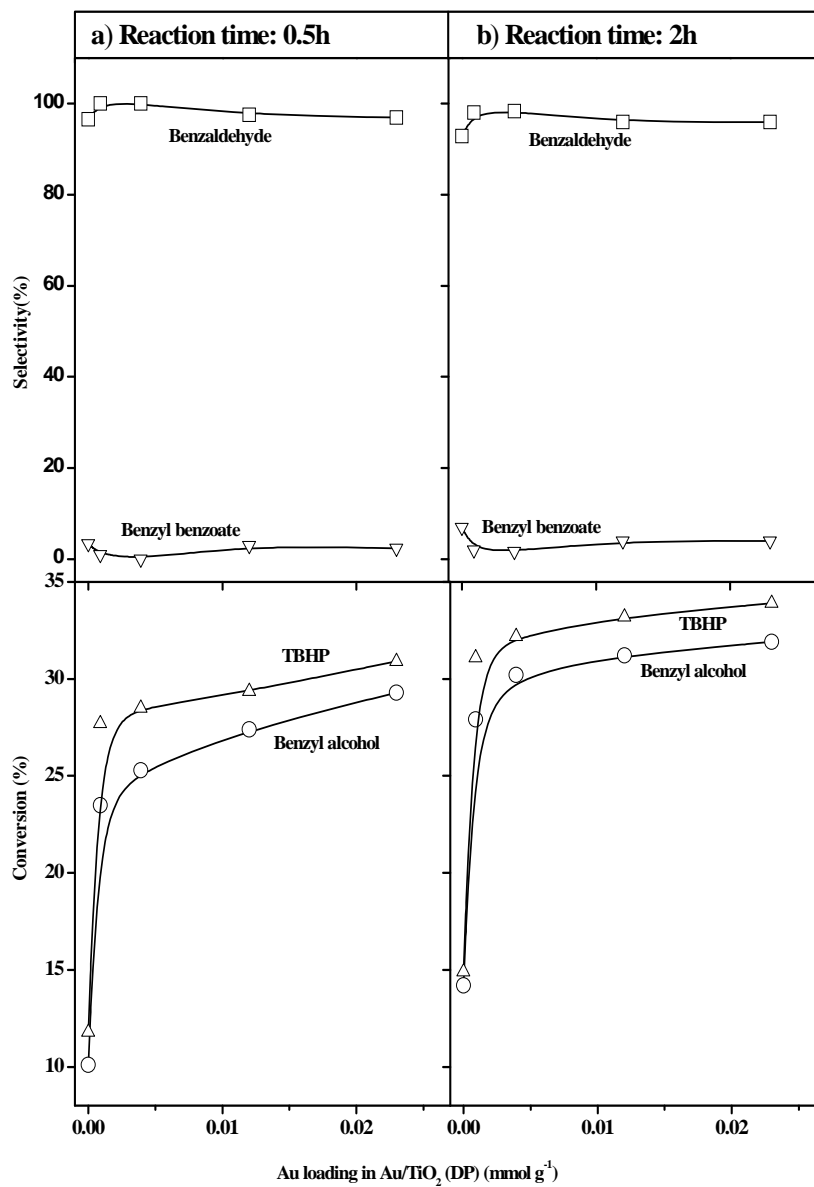
The observed binding energy shift in both the cases is in the range of 2.0 to 2.7 eV. This suggests the presence of gold in both the metallic ( $\text{Au}^0$ ) and cationic ( $\text{Au}^{3+}$ ) forms in both the  $\text{Au}/\text{TiO}_2$  (DP and HDP) catalysts, similar to that observed by Fu et al. [31] for  $\text{Au}/\text{CeO}_2$  catalyst. However, it may be noted that the surface  $\text{Au}^{3+}/\text{Au}^0$  ratio is much higher in case of the  $\text{Au}/\text{TiO}_2$  (HDP) (Table 4.3).

#### 4.4.2 Influence of Gold Deposition Method on the Catalyst Performance

Results showing performance of the  $\text{Au}/\text{TiO}_2$  catalysts prepared by both the DP and HDP methods and having different gold loadings, in the solvent-free oxidation of benzyl alcohol to benzaldehyde by TBHP for the reaction period of 0.5 and 2 h are presented in Figures 4.8 and 4.9. In the absence of any catalyst, the benzyl alcohol conversion was 14.3 % with 99 % selectivity for benzaldehyde.

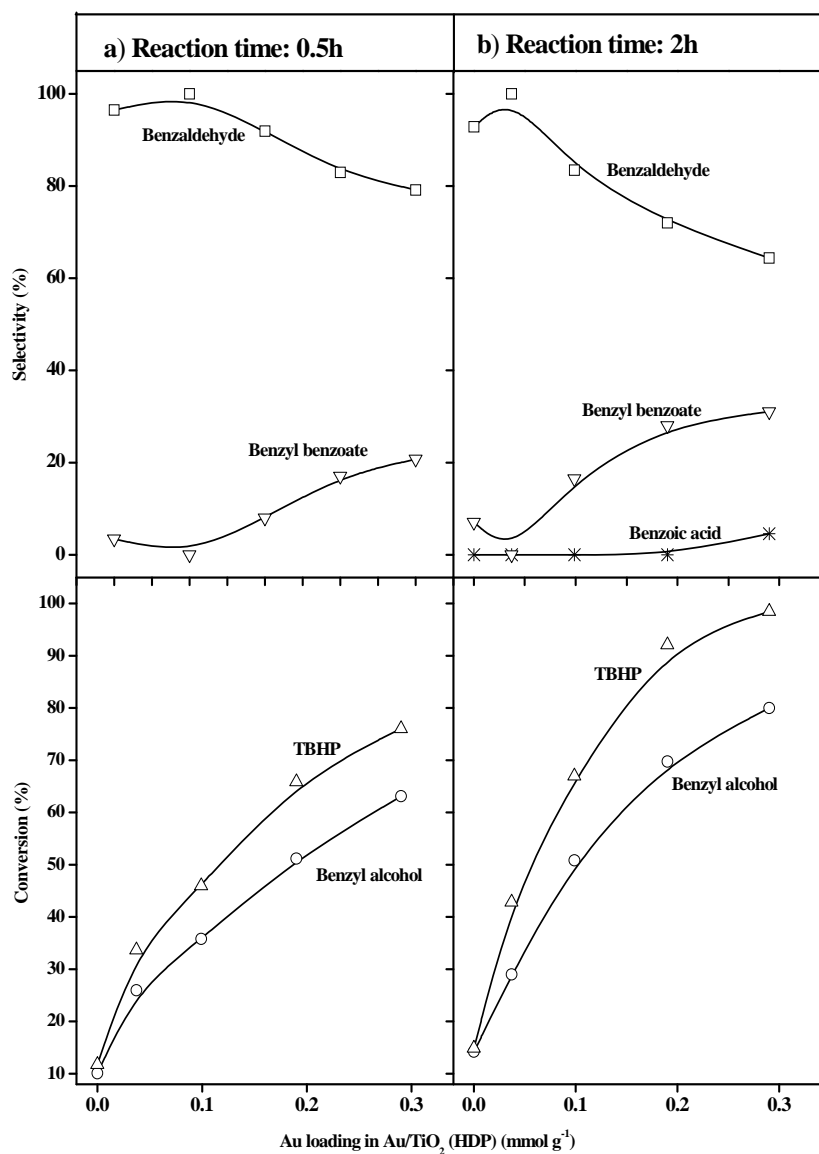
For both the catalysts (Figures 4.8 and 4.9), the conversion increased and the selectivity for benzaldehyde decreased with increasing the gold loading, depending upon the catalyst and the reaction period. The increase in the conversion of benzyl alcohol and TBHP is particularly sharp in the region of lower Au loading. The benzoic acid in the reaction products was observed only for the very high Au loading for the catalyst prepared by the HDP method.

The  $\text{Au}/\text{TiO}_2$  catalyst prepared by the HDP method, showed more catalytic activity in the benzyl alcohol oxidation because of their higher Au loading, lower Au particle size and/or their higher  $\text{Au}^{3+}/\text{Au}^0$  ratio (Table 4.3). The observed decrease in the benzaldehyde selectivity with increasing the Au loading is, however, expected because of the increase in the benzyl alcohol conversion. Also, since the TBHP/benzyl alcohol mole ratio in the reaction mixture is higher than 1.0, the results (Figures 4.8 and 4.9) indicating appreciable decomposition of TBHP over the  $\text{Au}/\text{TiO}_2$  catalysts simultaneously with the benzyl alcohol oxidation reaction.



**Figure 4.8:** Influence of Au loading in Au/TiO<sub>2</sub> (DP) catalyst on its performance in the oxidation of benzyl alcohol

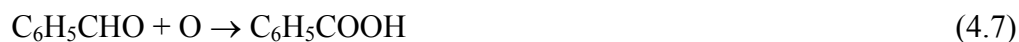
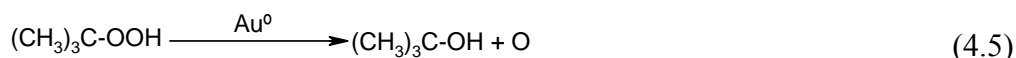




**Figure 4.9:** Influence of Au loading in Au/TiO<sub>2</sub> (HDP) catalyst on its performance in the oxidation of benzyl alcohol.

Since, the benzaldehyde is an intermediate product in the oxidation process; its selectivity is decreased with increasing the reaction time and consequently increasing the benzyl alcohol conversion.

The high benzyl alcohol oxidation activity of the Au/TiO<sub>2</sub> (HDP) catalyst is attributed to both the nano-size metallic gold (Au<sup>0</sup>) particles, particularly the low-coordinated Au atoms at corners and edges and the cationic gold species (Au<sup>3+</sup>) located at the interface between the TiO<sub>2</sub> support and the Au nanoparticles. On the nanosize metallic gold particles, decomposition of TBHP may lead to the formation of highly reactive atomic oxygen (O) species, responsible for the oxidation of benzyl alcohol to benzaldehyde and benzoic acid, involving following elementary reactions.



Because of the presence of easily reducible Au<sup>3+</sup> species in both the Au/TiO<sub>2</sub> (DP and HDP) catalysts, a redox mechanism, similar to that described in Chapter 3 for the oxidation of benzyl alcohol over MnO<sub>4</sub><sup>-1</sup>-exchanged hydrotalcite catalysts may also be operative simultaneously in the benzyl alcohol oxidation over the Au/TiO<sub>2</sub> catalysts.

## 4.5 OXIDATION OF BENZYL ALCOHOL OVER Au/MgO CATALYST

The Au/MgO catalyst showed highly promising performance in the benzyl alcohol to benzaldehyde oxidation and hence further detailed investigation on this catalyst has been carried out.

### 4.5.1 Influence of Au Deposition Method Used in Catalyst Preparation

The results showing the influence of the method of gold deposition (viz. DP, HDP and impregnation) on the gold loading (measured by ICP-OES), surface area and Au particle size

(measured by TEM) of the Au/MgO catalysts are presented in Table 4.4 and Figure 4.10. The catalytic performances of the Au/MgO catalysts in the oxidation of benzyl alcohol to benzaldehyde by TBHP are compared in Figure 4.11.

**Table 4.4:** Properties of Au/MgO catalysts, prepared by different methods.

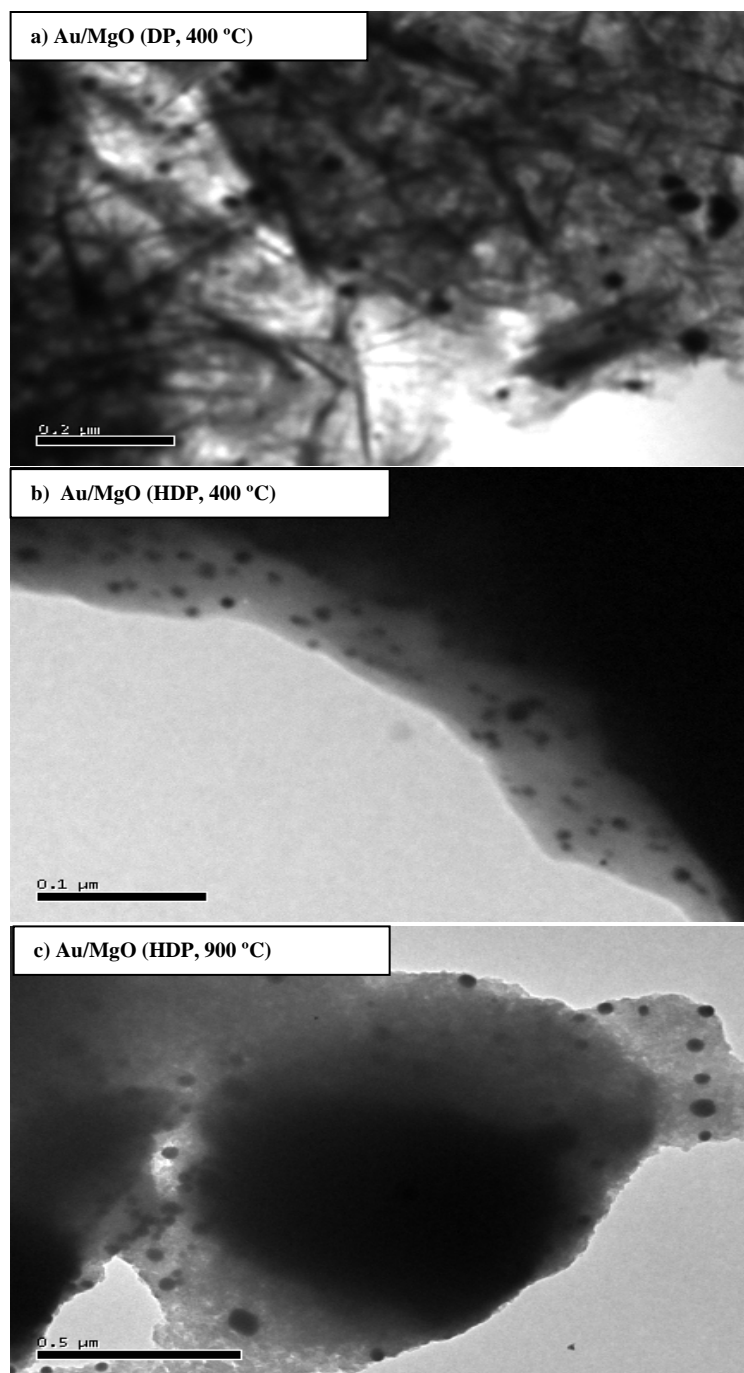
Method of preparation	Au loading by ICP (mmol. g <sup>-1</sup> )	Calcination temperature (°C)	Surface area (m <sup>2</sup> .g <sup>-1</sup> )	Au particle size (average) (nm)
HDP	0.38	400	47	6.2 (8.9) <sup>a</sup>
HDP	0.38	900	34	28
DP	0.21	400	49	19
Impregnation	0.41	400	40	31

<sup>a</sup> Measured by XRD for Au (200) peak ( $2\theta = 38.5^\circ$ ), HDP = Homogeneous Deposition Precipitation, DP = Deposition Precipitation.

The results in Table 4.4 and Figure 4.11 reveal that, as compared to the DP method, the HDP and impregnation methods provided much higher gold loading on the MgO support. The catalyst prepared by the HDP method shows much better performance than the catalysts prepared by the DP and impregnation methods.

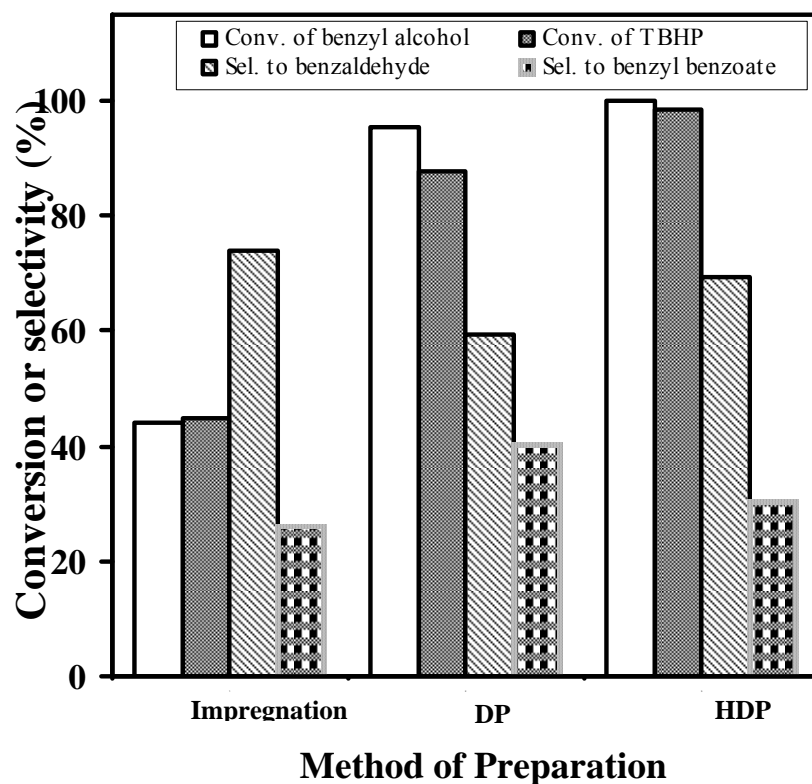
The higher Au loading in the Au/MgO catalyst prepared by HDP can be explained as follows. Continuous monitoring of the pH during the catalysts preparation by the DP and HDP methods showed that, in case of the Au/MgO catalyst preparation by DP, the pH of the gold solution-MgO slurry was increased from 9.4 to 9.7 at the end of the deposition. Whereas, when the HDP method was used, the pH of the slurry was decreased from 9.9 to 7.7. The colloidal gold particles formed upon the precipitation have a negative surface-charge [33]. The

isoelectric point (IEP) [which is also called point of zero charge (PZC)] of MgO and Mg(OH)<sub>2</sub> is close to  $12.2 \pm 0.2$  [34, 35]. Since the final pH in case of the HDP method is much lower



**Figure 4.10:** TEM photographs of a) Au (0.21 mmol g<sup>-1</sup>)/MgO (DP) 400 °C, b) Au (0.38 mmol. g<sup>-1</sup>)/MgO(HDP) 400 °C, c) Au (0.38 mmol.g<sup>-1</sup>)/MgO (HDP) 900 °C.

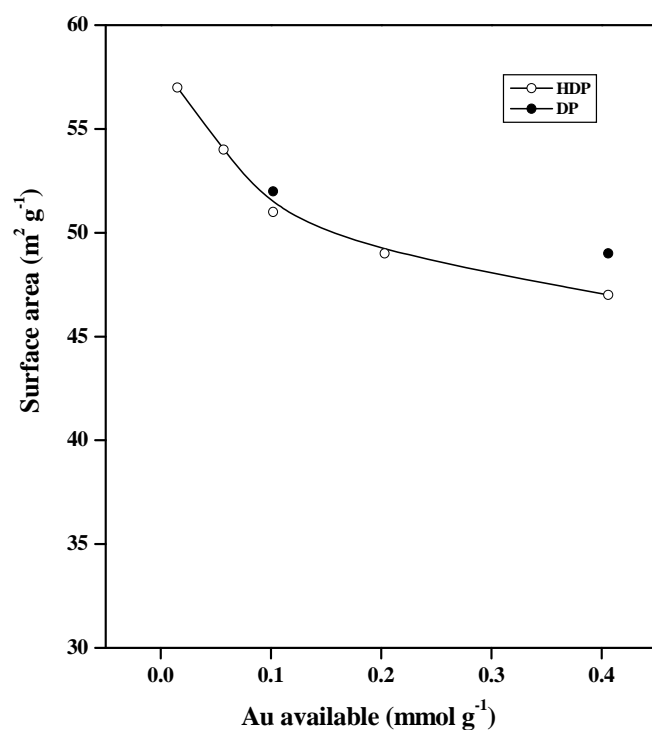
than the IEP of MgO and Mg(OH)<sub>2</sub>, most of the AuCl<sub>4</sub><sup>-</sup> anions from the solution are adsorbed on the positively charged surface of the MgO and Mg(OH)<sub>2</sub>, where the anions are hydrolyzed and precipitated on the surface, leading to a high gold loading. This is consistent with the observation made by Haruta and coworkers [36] that the gold loading on the support is higher if the pH is set in the range of 6 to 8.0. In the case of gold deposition on the MgO by the DP method, the final pH (9.7) was much higher than that observed in case of the HDP method (7.7) leading to a smaller adsorption of the AuCl<sub>4</sub><sup>-</sup> anions and consequently resulting in a lower gold deposition.



**Figure 4.11:** Performance of Au/MgO catalysts calcined at 400 °C and prepared by the different methods in the oxidation of benzyl alcohol to benzaldehyde by TBHP in absence of any solvent.

The performance of the Au/MgO catalysts for the benzyl alcohol conversion or benzaldehyde yield is in the following order Au/MgO (HDP) > Au/MgO (DP) > Au/MgO

(impregnation). In the impregnation method, the gold compound was deposited on the support by the incipient wetness technique and hence the gold loading in the resulting catalyst was the same as that available for the deposition. There was a complete deposition of the available gold on the support when HDP method was used. However, in case of the DP method, the gold deposition on the support was found to be about 60 % of that available. The poorer performance of the Au/MgO, prepared by DP, is expected due to its both the lower Au loading and larger Au particle size ( $D_{Au} = 19$  nm). The poorest performance of the Au/MgO prepared by the impregnation technique is expected mainly because of the higher gold particle size.



**Figure 4.12:** Correlation of Au available (mmol g<sup>-1</sup>) in catalyst and its surface area

The results showing the dependence of Au loading and surface area of Au/MgO (HDP) catalyst on the Au available for its deposition on the support during the Au deposition by the HDP method are shown in Figure 4.12.

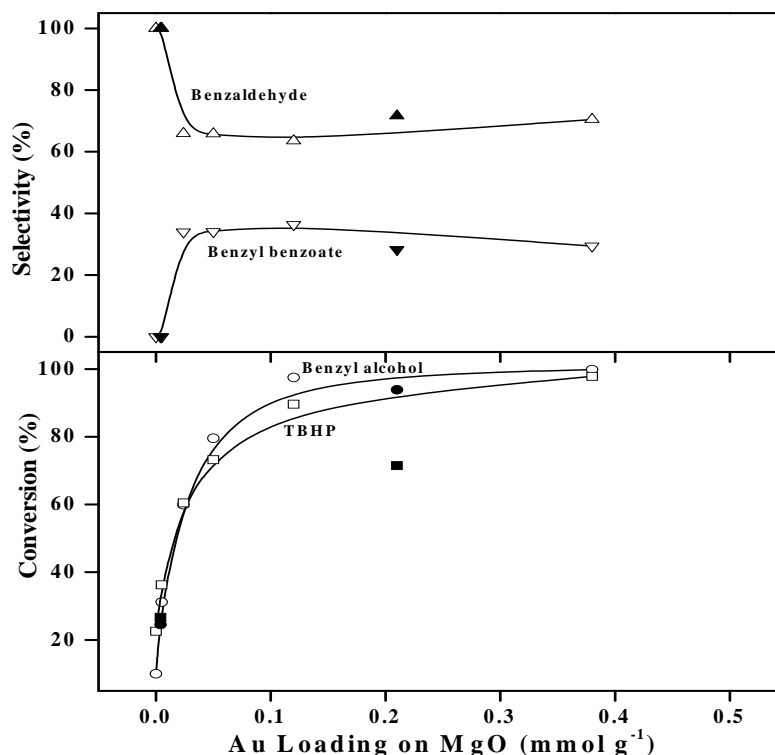
The Au loading increased, whereas, the surface area decreased markedly with increasing the Au available for its deposition on the support. The catalyst surface area decreased with increasing the Au loading. This may be because of the modification of the support surface during the gold deposition and calcination (at 400 °C).

## **4.5.2 Factors Influencing the Oxidation Reaction of Benzyl Alcohol by TBHP over Au/MgO (HDP)**

### ***4.5.2.1 Influence of Au Loading in Au/MgO (HDP) Catalyst***

The influence of the Au loading in the Au/MgO catalyst (prepared by the HDP or DP method) on its catalytic performance in the benzyl alcohol oxidation by TBHP is shown in Figure 4.13.

As expected, an increase in the benzyl alcohol conversion was observed with an increase in the Au loading. However, higher gold loading on the support also resulted in the small decrease in the benzaldehyde selectivity resulting in the formation of benzyl benzoate as the by-product. It may, however, be noted that the catalyst prepared by the HDP method shows higher activity than the one prepared by the DP method.



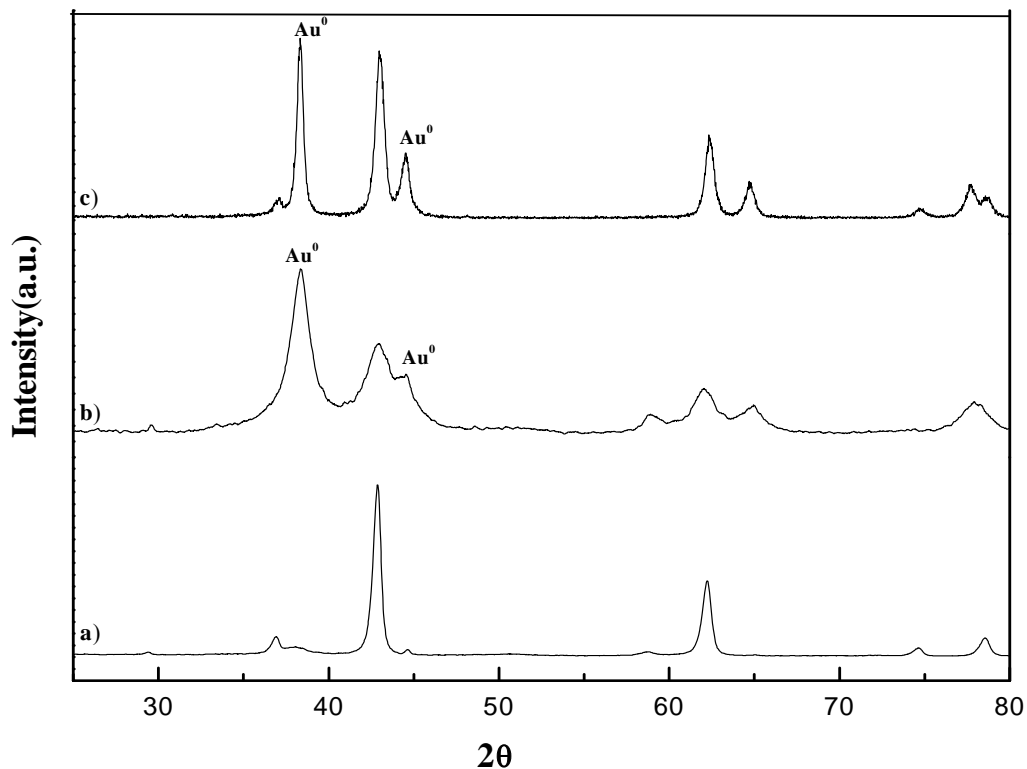
**Figure 4.13:** Influence of Au loading ( $\text{mmol}\cdot\text{g}^{-1}$ ) in the oxidation of benzyl alcohol to benzaldehyde by TBHP over Au/MgO (HDP) catalyst where [hollow symbol represents for Au/MgO (HDP) catalyst and solid symbol represents for Au/Mgo (DP) catalyst].

#### 4.5.2.2 Influence of Calcination Temperature of Au/MgO (HDP)

The XRD spectra of the MgO (calcined at  $400\text{ }^{\circ}\text{C}$ ) and Au ( $0.38\text{ mmol}\cdot\text{g}^{-1}$ )/MgO (HDP) calcined at different temperatures ( $400$  and  $900\text{ }^{\circ}\text{C}$ ) are presented in Figure 4.14.

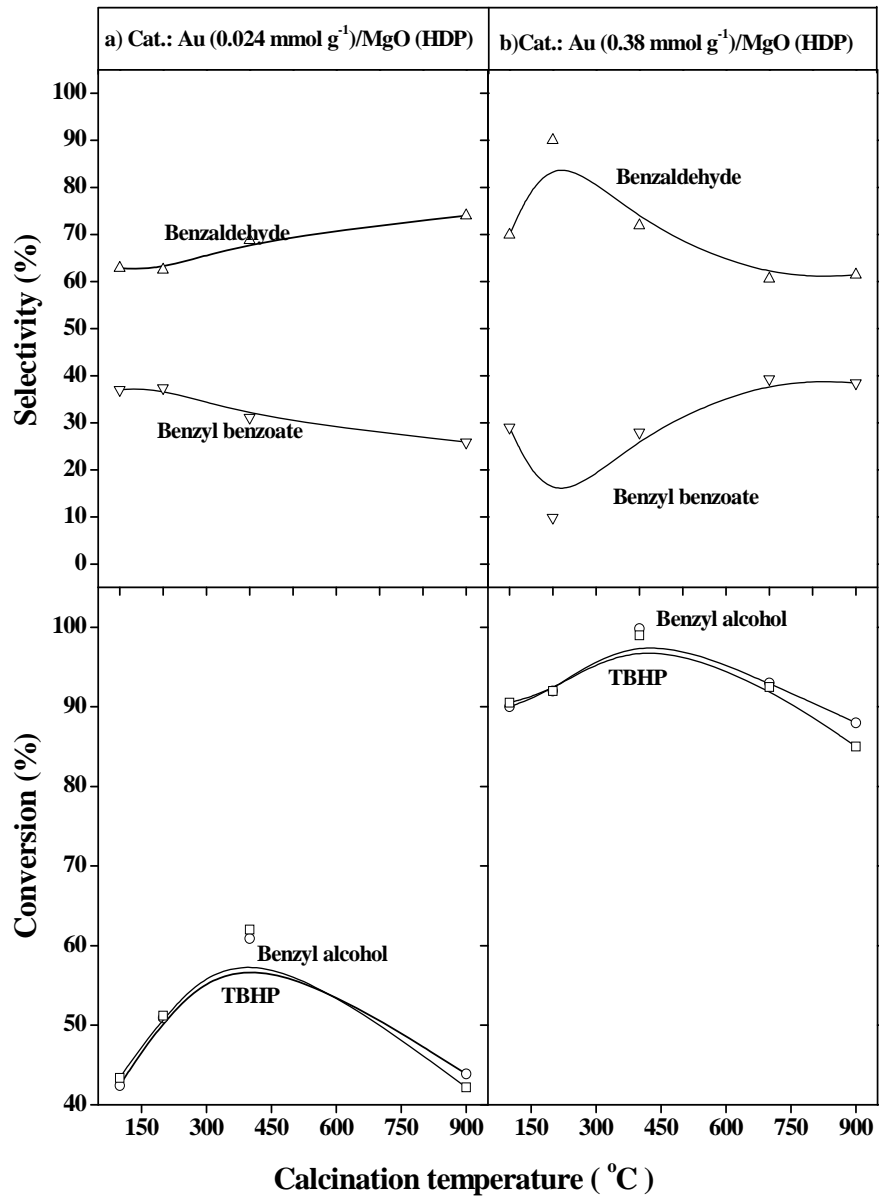
The TEM photographs of the Au ( $0.38\text{ mmol}\cdot\text{g}^{-1}$ )/MgO (HDP) catalysts calcined at the two different temperatures ( $400$  and  $900\text{ }^{\circ}\text{C}$ ) are already shown in Figure 4.10. The average Au particle size is increased from about  $6.2\text{ nm}$  to  $28\text{ nm}$  and the catalyst surface area is decreased from  $47$  to  $34\text{ m}^2\cdot\text{g}^{-1}$  with increasing the catalyst calcination temperature from  $400\text{ }^{\circ}\text{C}$  to  $900\text{ }^{\circ}\text{C}$ .





**Figure 4.14:** XRD of a) MgO (400 °C), b) Au/MgO (HDP, 400 °C, c) Au/MgO (HDP, 900 °C)

The results showing the influence of catalyst calcination temperature for two different Au/MgO (HDP) catalysts on their performance in the benzyl alcohol to benzaldehyde oxidation by TBHP are presented in Figure 4.15. The increase in the catalyst calcination temperature from 100 to 900 °C strongly influenced the conversion and product selectivity in the reaction, as follows:



**Figure 4.15:** Influence of catalyst calcination temperature on the oxidation of benzyl alcohol to benzaldehyde by TBHP over Au (0.38 mmol<sup>-1</sup>)/MgO (HDP) and Au (0.024 mmol<sup>-1</sup>)/MgO (HDP) catalyst.

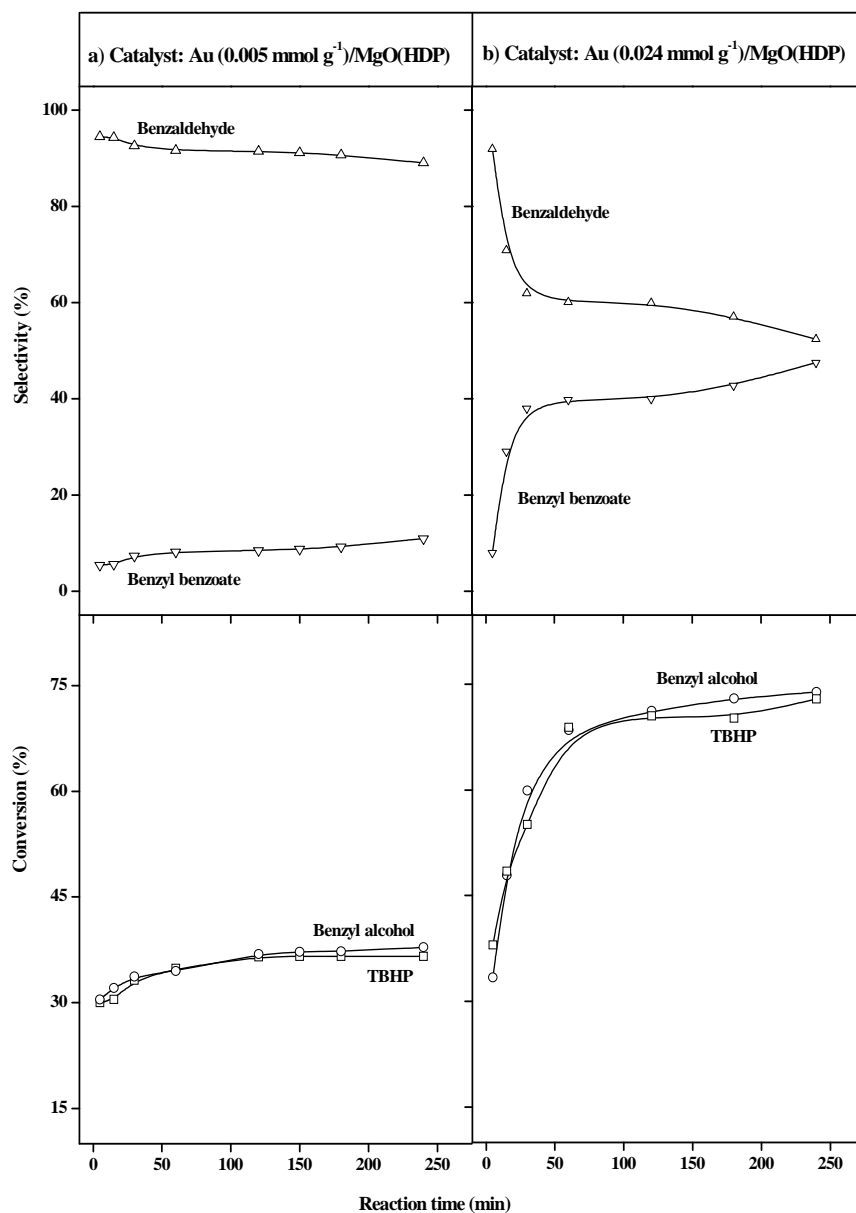
For the low and high Au loadings in the catalyst, the conversion of benzyl alcohol passed through a maximum with increasing the catalyst calcination temperature. However, the benzaldehyde selectivity passed through a maximum for the high Au loading but it increased continuously for the low Au loading.

This indicates that the optimum catalyst calcination temperature for obtaining the best performance (i.e. highest benzyl alcohol conversion and good benzaldehyde selectivity) in the oxidation reaction is 400 °C for the catalyst with both the low and high Au loadings. The poor catalyst performance at the lower catalyst calcination temperature (100 or 200 °C) is expected because of the presence of water and/or incomplete decomposition of the gold precursor compound deposited on the support during the homogeneous deposition precipitation. However, the increasingly poor performance at the higher catalyst calcination temperature (600-900 °C) is mainly due to the growth of larger gold particles (Table 4.4).

#### ***4.5.2.3 Influence of Reaction Conditions***

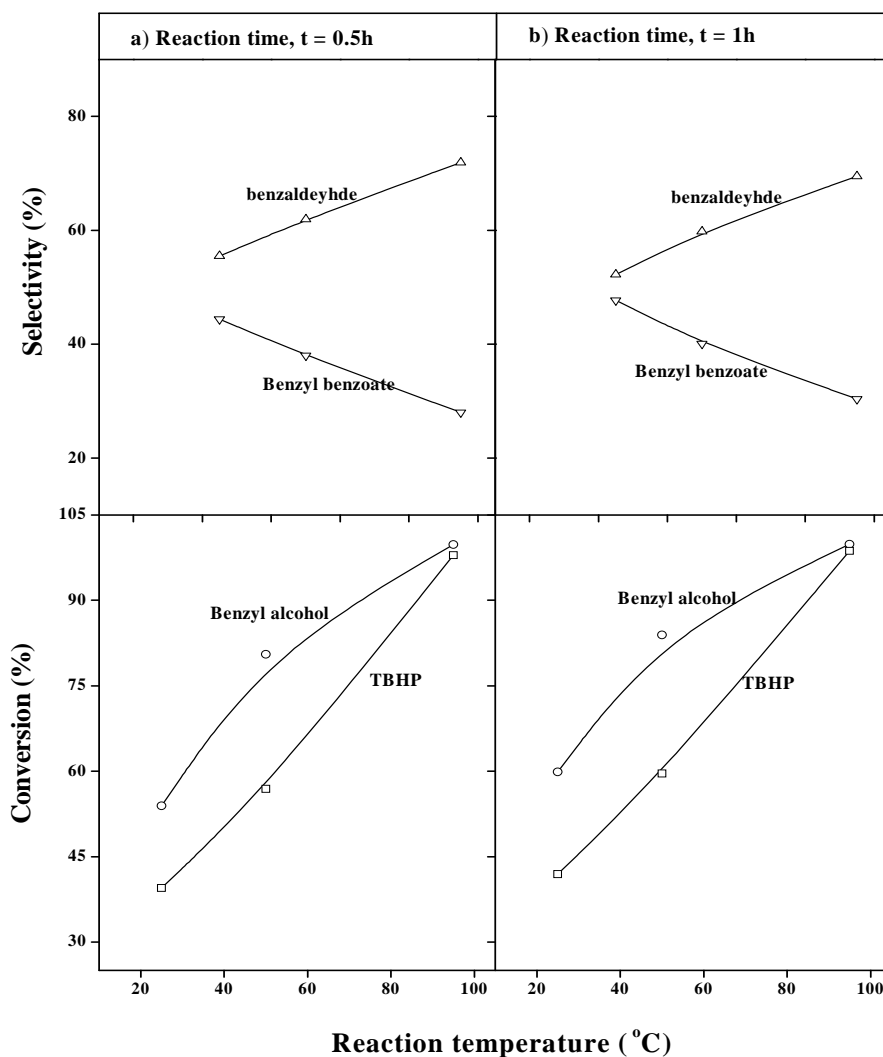
***Effect of reaction time:*** The Results showing the influence of reaction time in the oxidation reaction over the Au (0.005 mmol.g<sup>-1</sup>)/MgO (HDP) and Au (0.024 mmol.g<sup>-1</sup>)/MgO (HDP) catalysts are presented in Figure 4.16.

The benzyl alcohol conversion and selectivity for benzyl benzoate increased whereas the selectivity for benzaldehyde decreased with increasing the reaction period. The influence on the conversion and product selectivity is smaller for the catalyst with the lower Au loading.



**Figure 4.16:** Influence of reaction time on the oxidation of benzyl alcohol by TBHP to benzaldehyde over Au (0.005 mmol.g<sup>-1</sup>)/MgO (HDP) and Au (0.024 mmol.g<sup>-1</sup>)/MgO (HDP) catalyst.

**Effect of reaction temperature:** The results showing the influence of the reaction temperature on the conversion and selectivity in the oxidation reaction over the Au (0.38 mmol.g<sup>-1</sup>)/MgO(HDP) catalyst for two different reaction periods (0.5 and 1.0 h) are shown in Figure 4.17.



**Figure 4.17:** Influence of reaction temperature on the oxidation of benzyl alcohol by TBHP to benzaldehyde over Au (0.38 mmol g<sup>-1</sup>)/MgO (HDP) calcined at 400 °C (reaction time = 0.5 h and 1 h).

As expected, the benzyl alcohol conversion increased very markedly with increasing the temperature. The selectivity for benzaldehyde also increased appreciably and consequently that of benzyl benzoate decreased with increasing the reaction temperature.

The above results show that the Au/MgO (HDP) is a highly promising catalyst for the oxidation reaction.

#### **4.6 OXIDATION OF BENZYL ALCOHOL OVER Au/U<sub>3</sub>O<sub>8</sub> CATALYST**

Since the Au/U<sub>3</sub>O<sub>8</sub> catalyst also showed highly promising performance in the benzyl alcohol to benzaldehyde oxidation, it was interesting to carry out further detailed investigation on this catalyst. The influence of various Au deposition methods for the preparation of Au/U<sub>3</sub>O<sub>8</sub>, Au loading in the catalyst, catalyst calcination temperature and reaction conditions on the catalyst performance in the benzyl alcohol to benzaldehyde oxidation in absence of any solvent has been investigated.

##### **4.6.1 Influence of Au Deposition Method Used in Catalyst Preparation**

The results showing the influence of the method of gold deposition (viz. DP, HDP, CP and impregnation) on the gold loading (measured by ICP-OES), surface area and Au particle size (measured by TEM) of the Au/U<sub>3</sub>O<sub>8</sub> catalysts are presented in Figures 4.18-4.19 and Table 4.5. The performance of the Au/U<sub>3</sub>O<sub>8</sub> catalyst in the oxidation of benzyl alcohol by TBHP is compared in Figure 4.20.

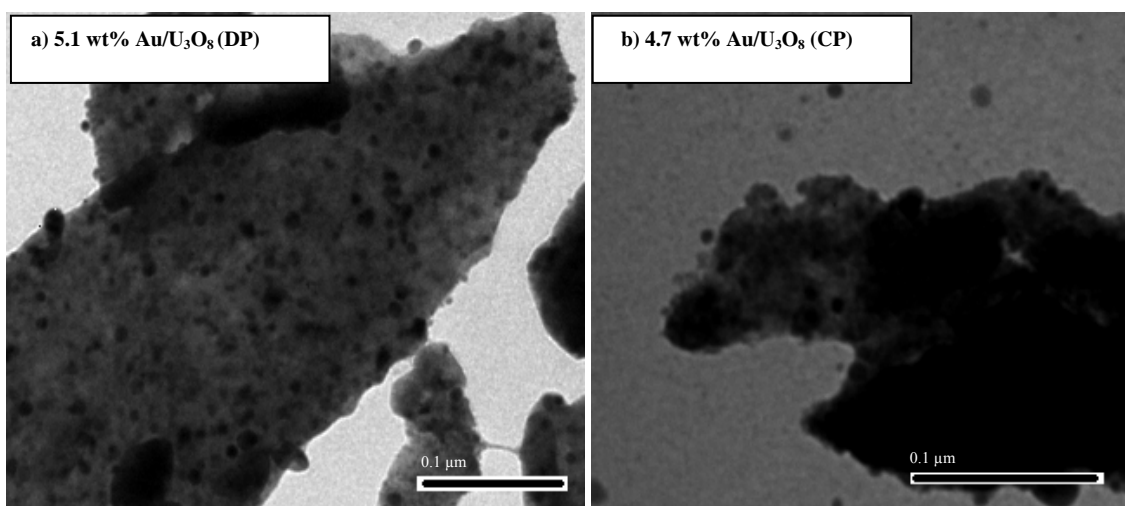
The results in Table 4.5 and Figures 4.18 and 4.19 reveal that, as compared to the DP and CP methods, the HDP and impregnation methods provided much higher gold loading on the U<sub>3</sub>O<sub>8</sub> support. The catalyst prepared by the HDP method shows much better performance than the catalysts prepared by the DP, CP and impregnation methods.

**Table 4.5:** Properties of Au/U<sub>3</sub>O<sub>8</sub> catalysts, prepared by different methods

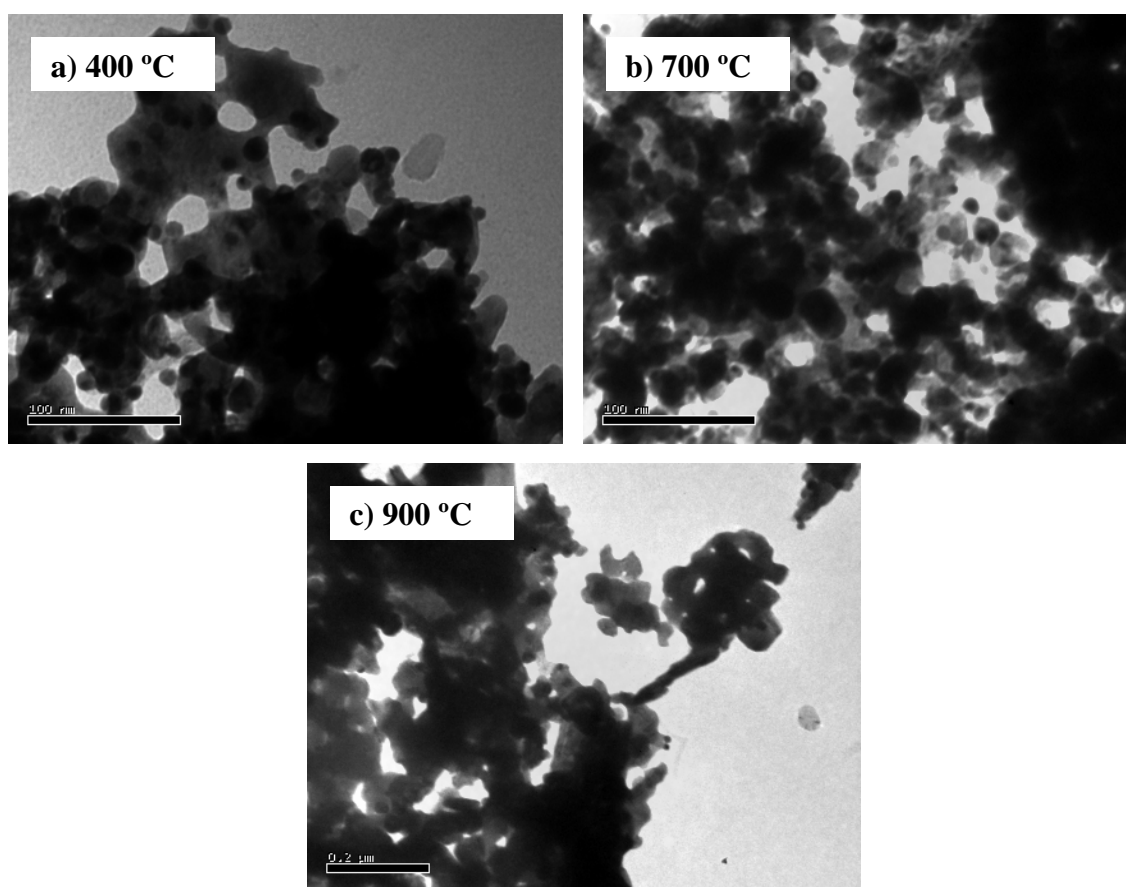
Method of preparation	Calcination temp. (°C)	Au loading (wt %) by ICP	Surface area (m <sup>2</sup> .g <sup>-1</sup> )	Particle size of Au (average)(nm)	
				TEM	XRD
HDP	400	8.0	6.5	9.4	11.5
DP	400	5.1	8.0	15.5	17.2
Co-precipitation	400	4.7	5.2	16	17.5
Impregnation	400	8.0	6.2	34.1	38.4
HDP	700	8.0	5.9	20.3	22.4
HDP	900	8.0	5.7	32.3	34.3

HDP = Homogeneous-Deposition Precipitation, DP = Deposition Precipitation,

The higher Au loading is observed in the Au/U<sub>3</sub>O<sub>8</sub> catalyst prepared by HDP (8 wt. %) with smaller particle size (9.4 nm) and the lower Au loading is observed in the Au/U<sub>3</sub>O<sub>8</sub> catalyst prepared by DP (5.1 wt.%) with larger particle size (15.5 nm) shown in Figures 4.18 and 4.19. respectively.

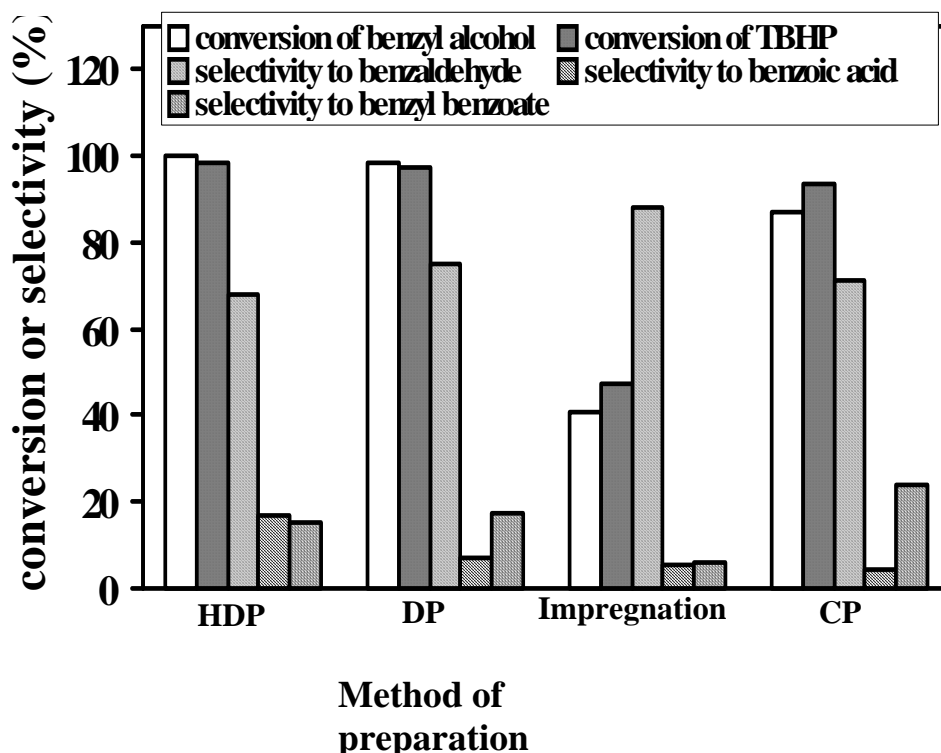


**Figure 4.18:** TEM photographs of a) Au/U<sub>3</sub>O<sub>8</sub> (DP, 400 °C), b) Au/U<sub>3</sub>O<sub>8</sub> (CP, 400 °C)



**Figure 4.19:** TEM photographs of Au/U<sub>3</sub>O<sub>8</sub> (HDP) catalysts calcined at a) 400 °C  
b) 700 °C and c) 900 °C.

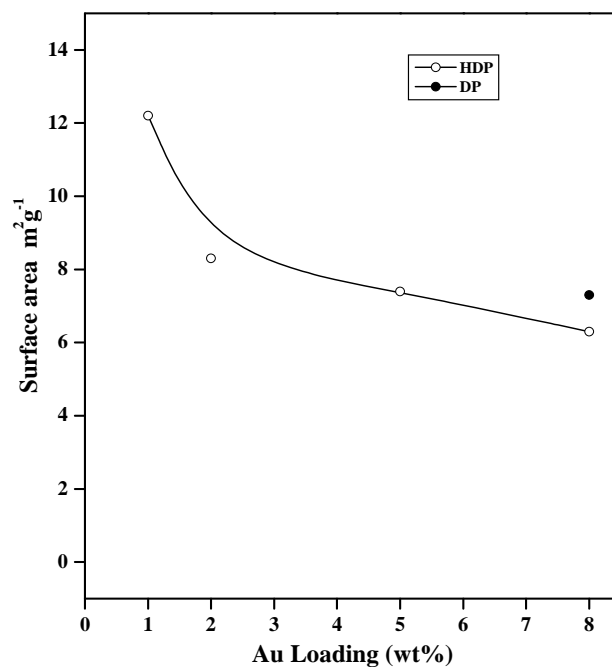




**Figure 4.20:** Performance of Au/U<sub>3</sub>O<sub>8</sub> catalysts calcined at 400 °C and prepared by the different methods in the oxidation of benzyl alcohol to benzaldehyde by TBHP in absence of any solvent

The performance of the Au/U<sub>3</sub>O<sub>8</sub> catalysts for the benzyl alcohol conversion or benzaldehyde yield is in the following order: Au/U<sub>3</sub>O<sub>8</sub> (HDP) > Au/U<sub>3</sub>O<sub>8</sub> (DP) ≥ Au/U<sub>3</sub>O<sub>8</sub> (CP) > Au/U<sub>3</sub>O<sub>8</sub> (Impregnation). In the impregnation method, the gold compound was deposited on the support by the incipient wetness technique and hence the gold loading in the resulting catalyst was the same as that available for the deposition. The much lower catalytic activity for the impregnation method may be due to the modification of the support surface by chloride anions during the impregnation (of the U<sub>3</sub>O<sub>8</sub> support with chloroauric acid) and calcination of the impregnated catalytic mass. The chloride anions (particularly at high concentration)

incorporated in the catalyst may also act as an inhibitor to the catalyst in the oxidation reaction of benzyl alcohol to benzaldehyde. There was a complete deposition of the available gold on the support when HDP method was used. However, in case of the DP and CP methods, the gold deposition on the support was found to be about 60 % of that available. The poorer performance of the Au/U<sub>3</sub>O<sub>8</sub> prepared by DP is expected due to its both the lower Au loading and larger Au particle size. The poorest performance of the Au/U<sub>3</sub>O<sub>8</sub> prepared by the impregnation technique is expected most probably because of the higher gold particle size.



**Figure 4.21:** Correlation of Au available (mmol.g<sup>-1</sup>) in catalyst and its surface area

In comparison the performance of the catalysts for the benzyl alcohol conversion is in the following order: Au/U<sub>3</sub>O<sub>8</sub> (HDP) > Au/U<sub>3</sub>O<sub>8</sub> (DP) ≥ Au/U<sub>3</sub>O<sub>8</sub> (CP) > Au/U<sub>3</sub>O<sub>8</sub> (Impregnation). The benzaldehyde selectivity for all the four different methods also found to be

the same order. The Results showing the dependence on the Au loading and surface area of Au/U<sub>3</sub>O<sub>8</sub> (HDP) catalyst of the Au available for its deposition on the support during the Au deposition by the HDP method and DP method are shown in Figure 4.21.

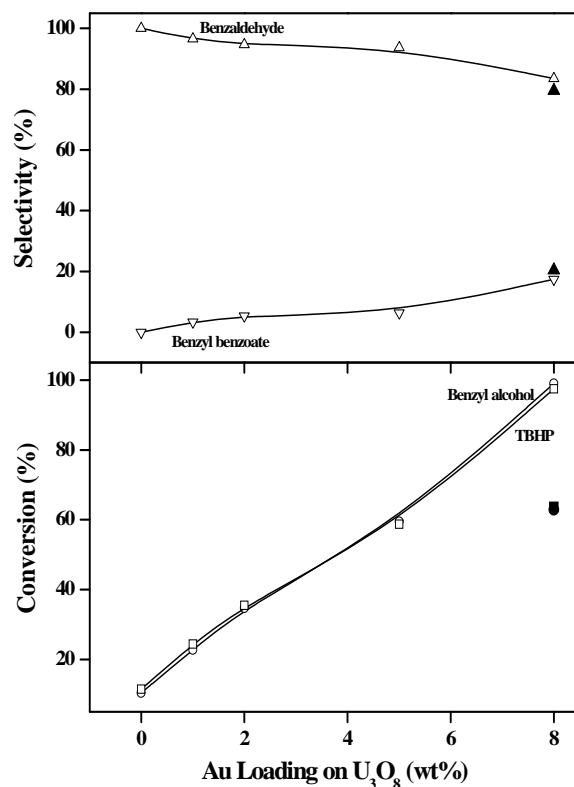
The Au loading is increased, whereas, the surface area is decreased markedly with increasing the Au available for its deposition on the support. The catalyst surface area is decreased with increasing the Au loading. This may be because of the modification of the support surface during the gold deposition and calcination (at 400 °C).

## **4.6.2 Factors Influencing the Oxidation Reaction of Benzyl Alcohol by TBHP over Au/U<sub>3</sub>O<sub>8</sub> (HDP)**

### ***4.6.2.1 Influence of Au Loading in Au/U<sub>3</sub>O<sub>8</sub> (HDP) Catalyst***

The influence of the Au loading in the Au/U<sub>3</sub>O<sub>8</sub> catalyst (prepared by the HDP and DP method) on its catalytic performance in the benzyl alcohol oxidation by TBHP is shown in Figure 4.22.

As expected, an increase in the benzyl alcohol conversion was observed with an increase in the Au loading. However, higher gold loading on the support also resulted in the small decrease in the benzaldehyde selectivity resulting in the formation of benzyl benzoate as the by-product. It may, however, be noted that the catalyst prepared by the HDP method shows higher activity than the one prepared by the DP method.

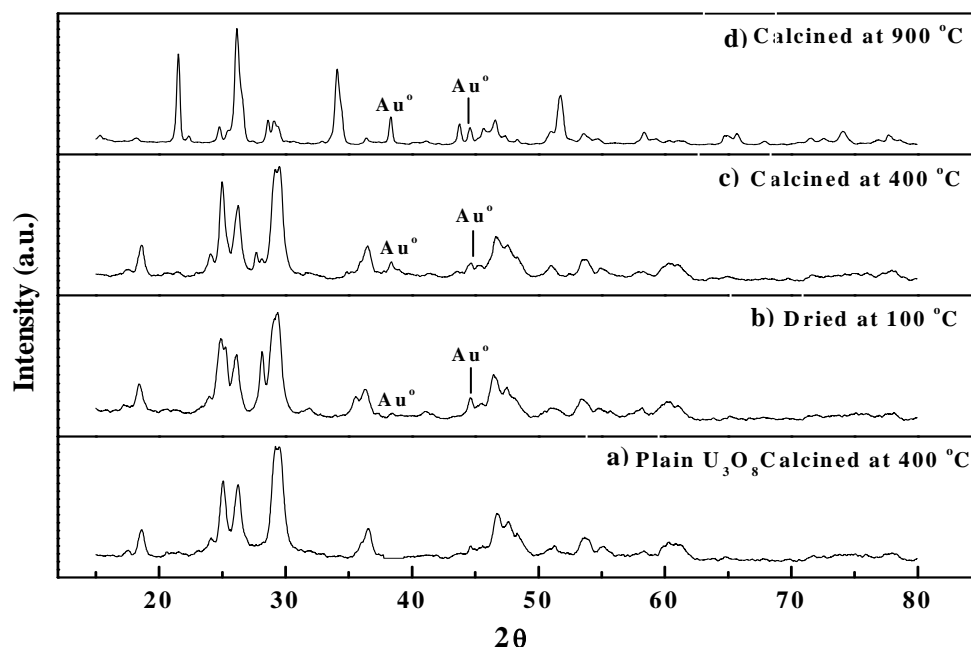


**Figure 4.22:** Influence of Au loading in the oxidation of benzyl alcohol by TBHP to benzaldehyde over  $\text{Au}/\text{U}_3\text{O}_8$  (HDP) catalyst where Hollow symbol represents for  $\text{Au}/\text{U}_3\text{O}_8$  (HDP) catalyst and Solid symbol represents for  $\text{Au}/\text{U}_3\text{O}_8$  (DP) catalyst.

#### 4.6.2.2 Influence of Calcination Temperature of $\text{Au}/\text{U}_3\text{O}_8$ (HDP)

XRD spectra of the  $\text{Au}$  (8 wt. %)/ $\text{U}_3\text{O}_8$  dried at 100 °C and calcined at different temperatures (400-900 °C) are presented in Figure 4.23.

The TEM photographs for the  $\text{Au}$  (8 wt. %)/ $\text{U}_3\text{O}_8$  (HDP) catalysts calcined at different temperatures (400, 700 and 900 °C) are already shown in Figure 4.19.

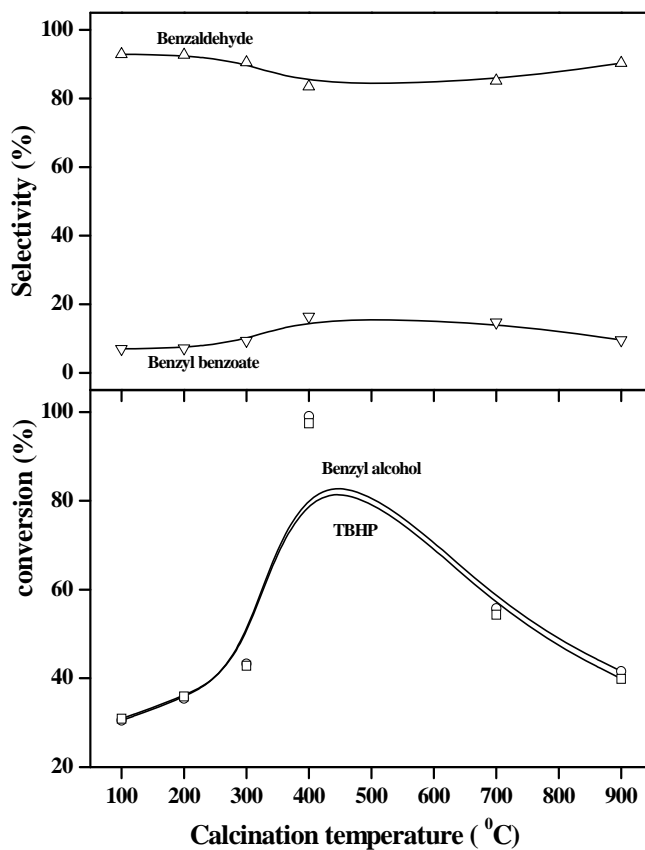


**Figure 4.23:** XRD of a) U<sub>3</sub>O<sub>8</sub> calcined at 400 °C and 8 wt.% Au/U<sub>3</sub>O<sub>8</sub> (HDP) catalysts calcined at b) 100 °C, c) 400 °C and d) 900 °C.

The average Au particle size increased from about 9.4 nm to 32.3 nm with the increase in the catalyst calcination temperature, which led to a small decrease in the surface area of the catalyst (Table 4.5).

The results showing the influence of calcination temperature of the two different gold loadings of Au/U<sub>3</sub>O<sub>8</sub> (HDP) catalyst on its performance in the benzyl alcohol to benzaldehyde oxidation by TBHP are presented in Figure 4.24. The increase in the catalyst calcination temperature from 100 to 900 °C has following influence on the conversion and product selectivity:

The conversion of benzyl alcohol passed through a maximum with increasing the catalyst calcination temperature. The influence on the product selectivity is, however, small.



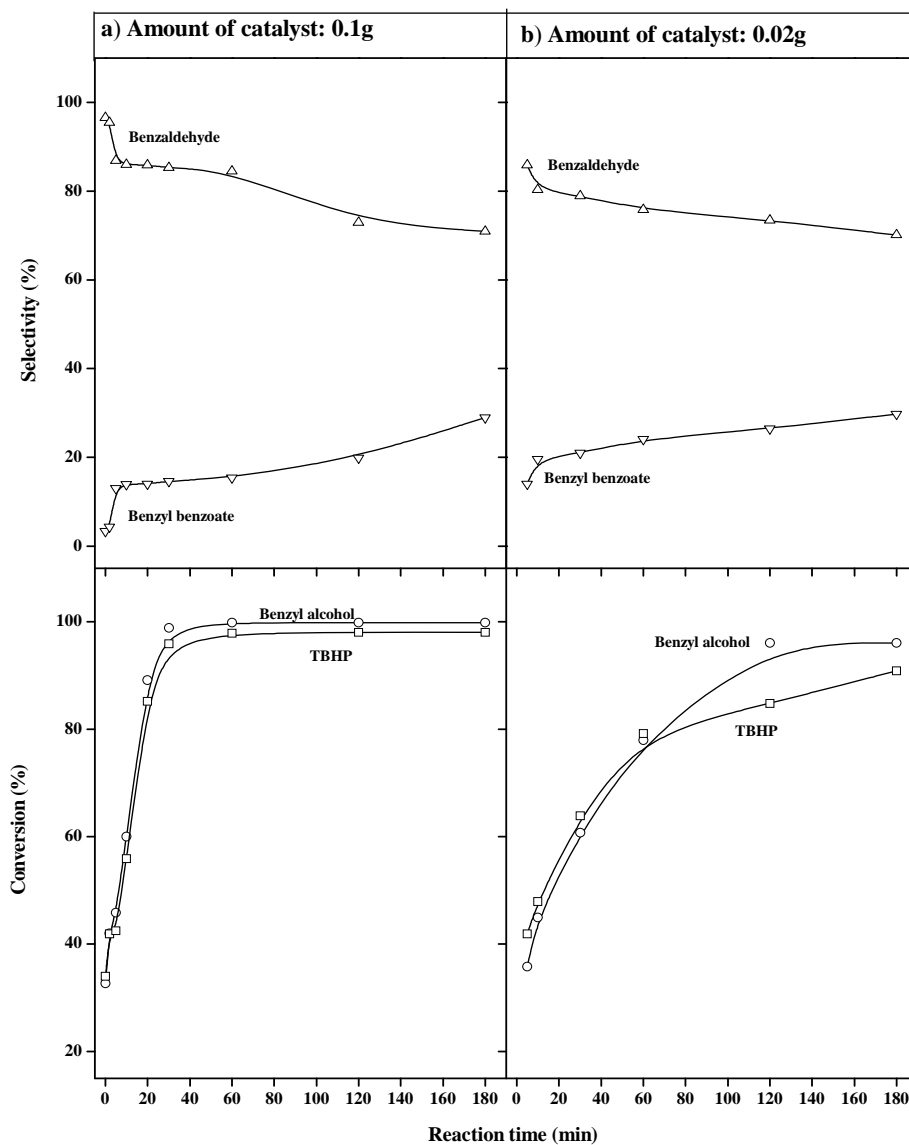
**Figure 4.24:** Influence of catalyst calcination temperature on the oxidation of benzyl alcohol to benzaldehyde by TBHP over Au (8 wt %)/U<sub>3</sub>O<sub>8</sub> (HDP).

This indicates that the optimum catalyst calcination temperature for obtaining the best performance (i.e. highest benzyl alcohol conversion and good benzaldehyde selectivity) in the oxidation reaction is 400 °C for the catalyst. The poor catalyst performance at the lower catalyst calcination temperature (100 or 200 °C) is expected because of the presence of water and/or incomplete decomposition of the gold precursor compound deposited on the support during the homogeneous deposition precipitation. However, the increasingly poor performance at the

higher catalyst calcination temperature (700-900 °C) is mainly due to the growth of larger gold particles (Table 4.5).

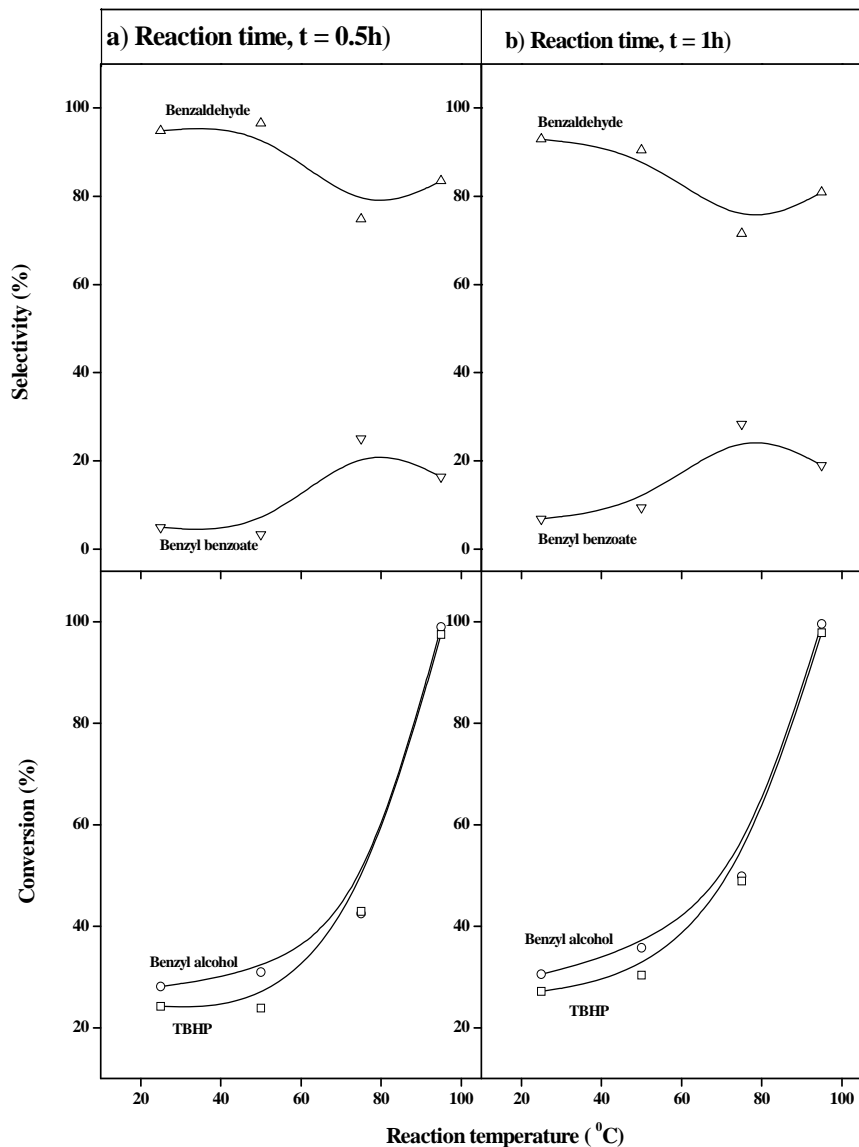
#### 4.6.2.3 Influence of Reaction Conditions

**Effect of reaction time:** The Results showing the influence of reaction time on the oxidation reaction over the Au/U<sub>3</sub>O<sub>8</sub> (HDP) catalyst is presented in Figure 4.25.



**Figure 4.25:** Influence of reaction time on the oxidation of benzyl alcohol by TBHP to benzaldehyde over Au (8 wt %)/U<sub>3</sub>O<sub>8</sub> (HDP)

The benzyl alcohol conversion and selectivity for benzyl benzoate increased whereas the selectivity for benzaldehyde decreased with increasing the reaction period.



**Figure 4.26:** Influence of reaction temperature on the oxidation of benzyl alcohol by TBHP to benzaldehyde over Au (8wt %)/U<sub>3</sub>O<sub>8</sub> (HDP) 400 °C (reaction time = 0.5 h and 1 h).



***Effect of reaction temperature:*** The results showing the influence of the reaction temperature on the conversion and product selectivity in the oxidation reaction over the Au (8 wt %)/U<sub>3</sub>O<sub>8</sub> (HDP) catalyst for two different reaction periods (0.5 and 1 h) are shown in Figure 4.26.

As expected, the benzyl alcohol conversion increased very markedly with increasing the temperature. The selectivity for benzaldehyde increased appreciably and consequently that of benzyl benzoate decreased with increasing the reaction temperature.

The above results showed that the Au/U<sub>3</sub>O<sub>8</sub> (HDP) is also a promising catalyst for the oxidation reaction.

#### **4.7 CONCLUSIONS**

This investigations leads to following important conclusions:

1. Among the supported gold catalysts, the Au/MgO (HDP) and Au/U<sub>3</sub>O<sub>8</sub> (HDP) catalysts showed excellent performance (benzyl alcohol conversion almost 99.9 %). The Au/TiO<sub>2</sub> (HDP) also showed a good activity in the oxidation of benzyl alcohol by TBHP.
2. The reaction products formed in the oxidation are benzaldehyde (major) and benzylbenzoate (minor). The benzoic acid formed in the oxidation is immediately reacted with benzyl alcohol over all the supported Au catalysts leading to the formation of benzylbenzoate.
3. Among the supported Au catalysts prepared by the different methods of gold deposition (i.e. DP, HDP, co-precipitation and impregnation), the catalysts prepared by the HDP method shows the best performance in the benzyl alcohol to benzaldehyde oxidation by TBHP in absence of any solvent.
4. There is no direct relationship exists between the surface properties of the metal oxide supports and the amount of gold deposited on them by the HDP method. However, the

particle size of the gold deposited on the metal oxides is found to be decreased with increasing the surface area of the support used in the catalyst.

5. For all the promising supported Au catalysts, their activity increased but their selectivity for benzaldehyde decreased with increasing the gold loading in the catalyst.
6. The observed higher catalytic activity of the Au/TiO<sub>2</sub> (HDP) catalyst as compared to that of Au/TiO<sub>2</sub> (DP) catalyst is expected because of its higher Au loading, lower Au particle size and/or higher surface Au<sup>3+</sup>/Au<sup>0</sup> ratio.
7. The performance of the supported Au catalysts (HDP) in the oxidation of benzyl alcohol is strongly influenced by gold loading, method of preparation and catalyst calcination temperature, reaction time and reaction temperature.

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## **CHAPTER 5**

### **C-C Coupling by the Heck Reaction Using Heterogeneous Catalysts**

## CHAPTER-5

# C-C Coupling by the Heck Reaction Using Heterogeneous Catalysts

### 5.1 BACKGROUND AND OBJECTIVE OF THE PRESENT WORK

Transition metal catalyzed carbon-carbon (C-C) coupling is one of the most important reaction in synthetic organic chemistry [1]. Palladium catalyzed C-C bond forming Heck reaction is one of them [2]. The recent applications of Heck reaction include the manufacture of Novartis' Prosulfuron<sup>TM</sup> - an agrochemical, octyl-p-methoxycinnamate - a sunscreen agent, Albemarle's naproxen - an antibiotic and Singulair - an antiasthma drug [3]. These transition metal catalyzed reactions have gained a steadily increasing importance in recent research and developments. Fine tuning of reaction parameters of known or newly discovered metal catalyzed transformations along with the catalyst development had a good impact on the synthesis of natural and non-natural biologically active compounds (valuable intermediates in the pharmaceutical and agrochemical industries) as well as theoretically interesting molecules. Palladium catalysis has achieved the status of an indispensable tool for both common and state of the art in organic synthesis.

The carbon-carbon bond forming reaction represents the potential application of palladium catalysts. Among the basic type of palladium catalyzed transformations, the Heck reaction and related chemistry occupy a special place and so it is considered as a sharpening stone of palladium catalysis. Palladium complexes with or without phosphine ligands can catalyze the Heck reaction. The phosphine-assisted approach is the classical and well-

established method, which gives excellent results in a majority of cases. Palladium catalyzed homogeneous reactions are often preferred for laboratory scale preparations and the majority of mechanistic elucidations and optimization studies have been carried out in solution phase. Frequently, however, problems are encountered when taking an optimized laboratory procedure and scaling it and most of the palladium catalyzed homogeneous reactions are notorious for air and moisture sensitivity, they deactivate fast and it is tedious and not an economical affair to recover and recycle the catalyst. The recent trend in catalysis related with environmental and economic concerns has resulted in much attention paid to heterogeneous palladium catalysts in which the Pd is immobilized on a solid support, making the catalyst easily recoverable from the reaction mixture with the possibility of reuse and waste minimization. For this reason the activity of Pd on its metallic complexes supported over variety of solid supports plays an important role in the reaction.

The palladium catalyzed Heck reaction of aryl halides and olefins is an important C-C bond forming reaction in organic synthesis. The reaction is generally catalyzed by either Pd (0) or Pd (II) complexes in solution [4]. There are a number of reports about use of heterogeneous catalysts for Heck reaction including the recent ones like LDH supported nanoplatinum [5], chitosan based heterogeneous catalysts [6], Pd-SAPO-31 [7], Pd-zeolites [8], Pd supported on metal oxides and zeolites [9], silica supported palladium catalysts [10], Ni, Co, Cu and Mn heterogeneous catalysts [11].

The zirconia supported palladium catalysts have been studied extensively for removing volatile organic compounds from industrial processes and automobile exhaust emissions by catalytic oxidation to harmless products like water and carbon dioxide [12-16], and for hydrodechlorination wherein polychlorinated organic substances, which are pollutants, can be converted into useful products [17,18].

Heck reaction is a tough challenge for designing recyclable systems and for that inorganic supports reported in the literature for the Heck reaction can be divided into three main types; microporous zeolites, mesoporous materials and clays. However, Djakovitch and Koehler [9, 19, 20, and 21] reported recently that the palladium supported on metal oxides and modified zeolites are highly active, selective and reusable catalysts for the Heck reaction of aryl halides with olefins and the authors relate that higher palladium dispersion leads to higher activity. Jacobs and co-workers [22] also reported Pd-zeolite and palladium supported on carbon and SiO<sub>2</sub> catalysts for the Heck reaction with high yields and also reported different states of Pd in the zeolites, i.e. Pd<sup>2+</sup> ions, PdO particles, and Pd<sup>0</sup> metal particles of different sizes. We have found that the heterogeneous catalyst containing palladium on zirconia is an efficient catalyst for the reaction between aryl halides and olefins to afford stilbenes in good yields. The objective of the present study was to (1) replace palladium with other transition metal-based catalysts, (2) eliminate the use of costly and non-recyclable catalytic system and (3) utilize heterogeneous, reusable catalyst in place of present homogeneous systems with higher activity.

## **5.2 CATALYSTS AND BRIEF EXPERIMENTAL PROCEDURES**

The supported Pd catalysts were prepared by different methods like impregnation, deposition-precipitation, homogeneous deposition-precipitation and co-precipitation methods. The catalyst preparation procedures are already discussed in Chapter 2, section 2.2.5. The general experimental procedure for carrying out the Heck reaction is given below.

To 5 ml of DMF, were added 2.5 mmol of aryl halide, 6.5 mmol of alkene, catalyst (10 wt % of aryl halide) and 7.23 mmol of base. The mixture was stirred at bath temperature 140 °C in nitrogen atmosphere for an appropriate time and the reaction was monitored by TLC. After

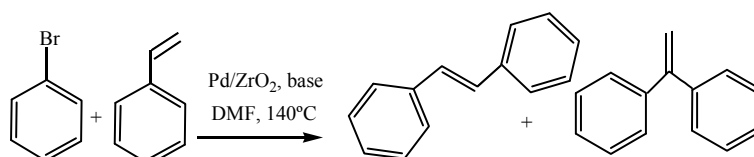


completion of reaction, the catalyst was separated by filtration and washed with DMF (3 x 3 ml). Then the filtrate was quenched with water followed by extraction with ethyl acetate to give the crude product, which was subsequently purified by column chromatography on silica gel with petroleum ether/ethyl acetate as eluent. The catalyst was further washed with acetone, dried and reused. The reaction products were isolated by column chromatography and were characterized by NMR, IR, Mass spectroscopy and elemental analysis.

### 5.3 RESULTS AND DISCUSSION

#### 5.3.1 Influence of the Catalyst Preparation Methods in the Heck Reaction

The Heck reaction of bromobenzene with styrene (Scheme 5.1) was carried out in DMF using supported palladium/zirconia catalysts prepared by different methods (viz. impregnation, deposition-precipitation, homogeneous-deposition-precipitation and co-precipitation methods) in presence of  $K_2CO_3$  for 12 h and the results obtained by gas chromatography analysis are shown in Table 5.1.



**Scheme 5.1**

It is interesting to note from the results (Table 5.1) that the method of Pd deposition on the support has strong influence on the conversion in the Heck arylation of styrene with bromobenzene. The results showed that the impregnation method produced the best catalysts. This may be due to higher palladium loading on the support surface thus providing higher active sites. For the catalysts prepared by the other methods, the best results were obtained with

the catalyst prepared by the HDP method. This is likely because of the higher dispersion of Pd on the support and also due to the higher loading as compared to the catalysts prepared by DP and CP methods.

**Table 5.1:** Influence of method of Pd/zirconia catalyst preparation on the arylation of styrene with bromobenzene [reaction conditions: 2.5 mmol bromobenzene + 6.5 mmol styrene + 5 ml DMF + 7.23 mmol K<sub>2</sub>CO<sub>3</sub> + catalyst (10 wt % of aryl halide), bath temperature = 140 °C and reaction time = 12 h]

Catalyst preparation method	Surface area (m <sup>2</sup> g <sup>-1</sup> )	Conversion (%)		
		Bromobenzene	Stilbene	DPE
HDP	73.3	52.0	87.7	12.2
DP	78.5	30.5	90.9	9.0
Co-precipitation	73.1	40.7	86.9	13.0
Impregnation	68.0	79.9	93.5	6.4
ZrO <sub>2</sub> <sup>a</sup>	86.0	3.1	96.8	3.1

<sup>a</sup> support ZrO<sub>2</sub> (without Pd), DPE = 1, 1'-Diphenylethylene

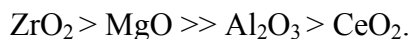
In all cases, the product formed was mainly a mixture of *trans*-stilbene and 1,1'-diphenyl ethylene, formed in very small amount, as compared to typical homogeneous systems (palladium acetate + P(C<sub>6</sub>H<sub>5</sub>)<sub>3</sub>). In the reaction with pure zirconia (i.e. in the absence of Pd), the conversion of bromobenzene was 3.1%, even after 12 h. Among all the supported palladium catalysts prepared by different methods, the palladium/zirconia (impregnation) catalyst showed

the best performance, high activity for both bromobenzene and styrene and selectivity for stilbene in the Heck reaction.

### 5.3.2 Influence of Different Supports Used in the Supported Pd for the Heck Reaction

Results for different supported palladium catalysts (viz. Pd/ZrO<sub>2</sub>, Pd/MgO, Pd/Al<sub>2</sub>O<sub>3</sub> and Pd/CeO<sub>2</sub>), all prepared by impregnation method, in the Heck reaction of bromobenzene with styrene are shown in Table 5.2. The results show that the support in the supported Pd catalyst plays a crucial role in deciding the activity of the catalyst in the reaction.

A following order of the supports is shown for the best performance of the supported Pd catalyst for arylation of styrene with bromobenzene.



The loading of palladium on MgO support was also studied and the results are included in Table 5.2. The results suggest that the Pd loading on the support has only a small effect on the conversion and/or selectivity in the reaction.

This is consistent with that observed earlier for Pd supported on mesoporous silica [23]. It may be noted that, with the Pd/mesoporous silica, in spite of the high Pd dispersion due to very sophisticated catalyst preparation technique and also the use of expensive Si-MCM-41, as a support, only 39 % conversion was achieved at 170 °C and 48 h reaction time. However, the catalyst (Pd/ZrO<sub>2</sub>) used in the present work is much superior to Pd/Si-MCM-41.

It is reported in the literature that the Pd on basic support is more suitable for the activation of aryl halides [24, 25]. This seems to be true to some extent in our case, because more acidic supports such as CeO<sub>2</sub> and Al<sub>2</sub>O<sub>3</sub> are less active than zirconia and basic MgO supports.

**Table 5.2:** Influence of different supports used in palladium catalysts for their performance in arylation of styrene with bromobenzene [reaction conditions: 2.5 mmol bromobenzene + 6.5 mmol styrene + 5 ml DMF + 7.23 mmol K<sub>2</sub>CO<sub>3</sub> + catalyst (10 wt % of aryl halide), bath temperature 140 °C and reaction time = 12 h]

Catalyst Composition	Conversion	Product Selectivity	
	(%)	(%)	
	BBZ	Stilbene	DPE
Pd (2.5 wt. %)/ZrO <sub>2</sub>	79.9	93.5	6.4
Pd(2.5wt.%)-Cu (2.5%)/ZrO <sub>2</sub>	41	92.5	7.4
Pd (2.5 wt. %)/MgO	37	94	6
Pd (5 wt. %)/MgO	40	92.5	7.4
Pd (2.5 wt. %)/Al <sub>2</sub> O <sub>3</sub>	32.5	95.7	4.2
Pd (2.5 wt. %)/CeO <sub>2</sub>	22.5	97.9	2

BBZ = Bromobenzene, DPE = 1, 1'-Diphenylethylene.

Among the different supported Pd catalysts, Pd (2.5 wt.%)/ZrO<sub>2</sub> (prepared by impregnation method followed by its reduction with hydrazine), gave excellent results (79.9 % conversion with 93.5 % stilbene selectivity) in the Heck reaction of aryl bromide with styrene. However, the other catalysts showed poorer performance in comparison of this catalyst. Addition of co-metal (Cu) to Pd/ZrO<sub>2</sub> led to decrease in the overall performance of the catalyst possibly due to decrease of Pd loading and/or because of the modification of the active Pd sites by a co-metal.

### 5.3.3 Test for Heterogeneity of Reaction

The catalyst Pd/zirconia (10 wt % w.r.t.aryl halide), bromobenzene, styrene and base (as per their mole ratios described above) were mixed with DMF in nitrogen atmosphere with

constant stirring for 1 h. The catalyst was removed from the hot reaction mixture after the reaction period of 1 h and then the reaction was continued for a further period of 11 h. A little conversion (5.66 %) was observed after 12 h. This showed that the reaction did not proceed after the removal of the solid catalyst from the reaction mixture, clearly indicating that the reaction requires heterogeneous catalyst in order to result in the formation of desired product with high yield. This clearly shows that the reaction is heterogeneous one; it is not catalyzed by the dissolved catalyst components, if any.

#### **5.3.4 Catalyst Stability-Detection of Pd Leaching**

Palladium leaching (if any) from the palladium catalyst in the reaction medium, after the reaction was determined by the standard procedure of adding an aqueous ethanolic dimethylglyoxime (1 %) solution to a 5 ml of filtrate obtained by filtering the reaction mixture [26]. The solution has to be allowed to stand for long period (1 h) and formation of yellow orange precipitate of palladium dimethylglyoximate indicates the presence of palladium (in trace amounts) in the reaction mixture. However, in our case, Pd leaching was not observed during the reaction.

#### **5.3.5 Use of Pd/zirconia Catalyst for the Synthesis of Substituted Styrenes and Biologically Active Compounds like Substituted *trans*-stilbenes**

The C-C bond forming reactions play a vital role in the synthetic organic chemistry and the Heck reaction is one of them. The Pd/ZrO<sub>2</sub> used in the present work has been found to be an effective catalyst for the Heck reaction and substituted *trans*-stilbene was obtained in good yield, including biologically active natural products, by reaction of aryl halides with olefins.

Substituted stilbenes constitute an important group of biologically active compounds exhibiting significant anticancer activity [27]. Some of the stilbenes exhibit antifungal activity [28], while some are used as an intermediate for fluorescent brighteners and dyes [29],

antibiotics [30], cyclooxygenase-2 inhibitors [31] *etc.* The inhibitory effects on ethoxyresorufin o-deethylation (EROD) by *trans*-stilbene compounds were determined in bicistronic bacterial membranes containing human CYP1A1, CYP1A2 and CYP1B1 [32, 33]. Isolation of various combretastatins, from the South African tree *Combretum caffrum*, and the significant antitumor activity exhibited by combretastatin A-4, has resulted in the publication of a number of papers reporting synthetic as well as biological aspects of substituted stilbenes. A large number of combretastatin A-4 analogues have been synthesized and checked for the anticancer activity. Generally the *cis* stilbenes are more potent than the corresponding *trans* isomers though some of the *trans*-stilbenes exhibit significant antimitotic and antileukemic properties [34]. The biological activity exhibited by stilbenes keeps on attracting the synthetic organic chemistry community to explore alternative methods for their synthesis to make these compounds available in larger quantities for biological studies. The stilbene skeleton could be constructed by Wittig reaction between an aromatic aldehyde and benzylic phosphonium ylide. However, semistabilized ylide, like benzyl ylide, usually provides a mixture of *Z* and *E* isomers [35, 36] as well as triphenylphosphine oxide as a by-product that necessitates chromatography or crystallization for purification. Some researchers have employed the Horner-Wadsworth-Emmons reaction [37] for the synthesis of the *trans*-stilbenes [38, 35].

A number of studies have been reported for the preparation of the styrenes and mainly include Wittig reaction [27a, 27b, 27f, 39] while preparation of stilbene is best achieved by Heck reaction [40]. They are also prepared by reaction of benzyl sodium and benzaldehyde [29], reductive metalation of benzaldehyde dimethyl acetal [30], LDA-mediated condensation of benzyl bromides [41a], condensation of benzaldehydes and nitrotoluenes [41b], Knoevenagel condensation [41c] *etc.*

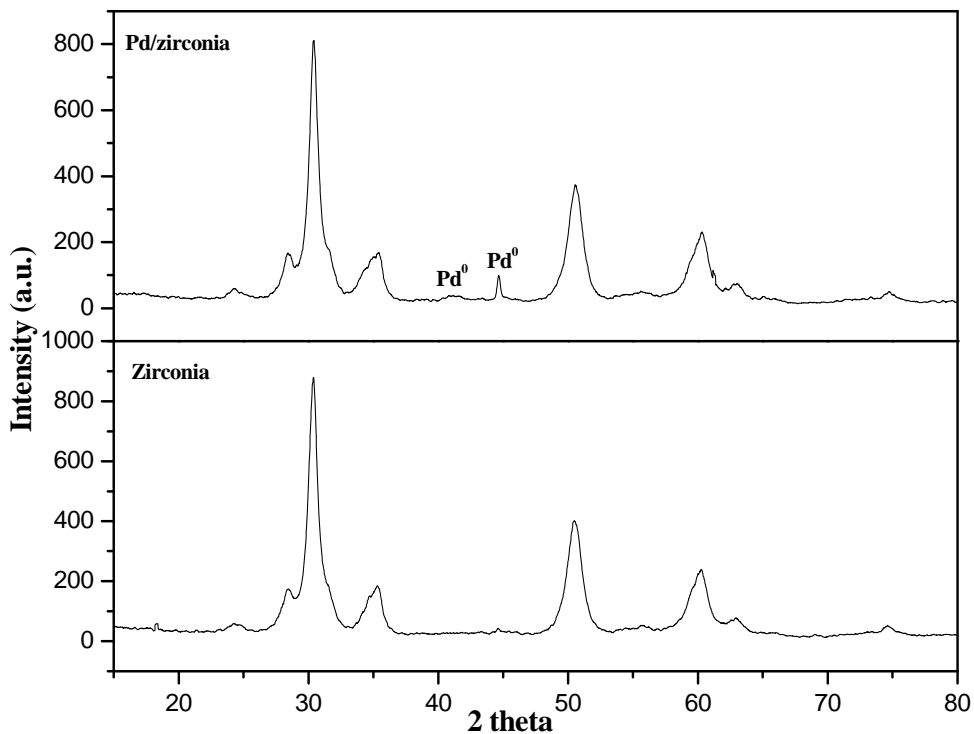
In the present work, palladium on zirconia has been found to be an effective catalyst in the synthesis of various substituted styrenes and stilbenes, including biologically active natural products, by reaction of aryl halides with olefins. The significant biological activity exhibited by stilbenes keeps on attracting the synthetic organic chemistry community to explore alternative methods for their synthesis to make these compounds available in larger quantities for biological studies.

### **5.3.6 Characterization of the Catalyst**

Among all the catalysts, Pd (2.5 wt %)/ZrO<sub>2</sub>, prepared by impregnation method followed by reduction with hydrazine gave excellent results in the Heck reaction of aryl bromide with styrene.

The catalyst was characterized by X-ray powder diffraction (using a Holland Phillips Diffractometer PW/1730 series X-ray generator with CuK $\alpha$  radiations) for the bulk Pd species (Pd<sup>0</sup> or PdO), Surface area of the catalyst was measured using a Monosorb Surface Area Analyzer (Quantachrome Corp., USA) based on the dynamic adsorption/desorption technique. The catalyst was also characterized by TEM (using a JEOL model 1200EX with CCD camera instrument) for particle size. The sample for TEM studies was prepared by placing a drop of an acetone suspension of the catalyst on a carbon coated copper grid.

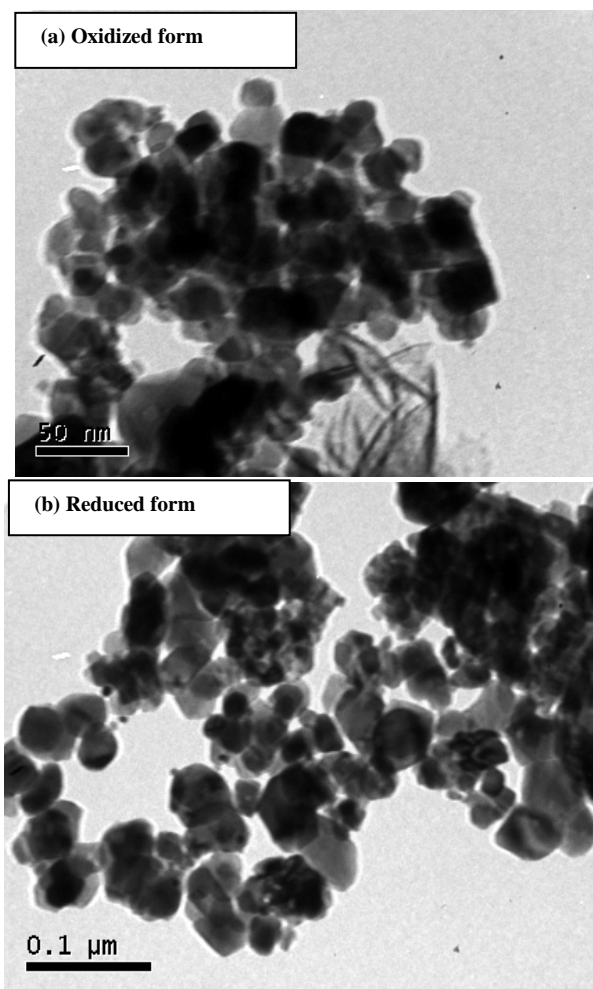
The X-ray diffraction patterns for the palladium/zirconia catalyst are presented in the Figure 5.1. The peak for Pd is seen at  $2\theta = 40^\circ$  and  $45^\circ$  indicating the presence of metallic palladium phase in the reduced catalyst. The particle size of Pd in the palladium/zirconia catalyst was found to be about 19.5 nm, obtained from Pd peak broadening.



**Figure 5.1:** XRD spectra of (2.5 wt %) Pd/zirconia catalyst calcined at 500 °C in air and reduced with hydrazine solution.

The TEM photographs of Pd/zirconia catalyst (prepared by the impregnation method) in oxidized form are presented in Figure 5.2a; it provides the direct observation of the morphology and distribution of Pd nanoparticles in Pd/zirconia catalyst. The pretreatment to Pd/zirconia in air at 500 °C followed by its reduction with hydrazine caused redispersion of Pd as shown in Figure 5.2b. The TEM image shows quite uniform Pd particles. The Pd nanoparticles are evenly dispersed on the oxide support. The TEM picture of these particles indicated the presence of metallic Pd with particle size of about 16 nm, which is close to that (19.5 nm) obtained from the XRD peak broadening.





**Figure 5.2:** a) TEM photograph of Pd/zirconia catalyst calcined at 500 °C in oxidized form  
b) TEM photograph of Pd/zirconia catalyst calcined at 500 °C in air and reduced with hydrazine solution.

### 5.3.7 Influence of Different Reaction Parameters in the Heck Reaction

We have also carried out the Heck reaction for 4-iodoanisole and acryl amide in presence of the Pd/ZrO<sub>2</sub> catalyst, and it showed very good activity in the reaction. The activity of the catalyst was found to be very good in the Heck reaction of bromobenzene and styrene, so it was interesting to carry out further detailed investigation on this catalyst by studying the

influence of various other substrates, solvents, bases, reaction time and reaction temperature on the catalytic performance in the reaction.

### 5.3.7.1 Effect of Different Bases

Among the various bases NaOAc, Na<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub> and zinc dust (inorganic base) pyridine, Et<sub>3</sub>N and Bu<sub>3</sub>N (organic bases) screened, K<sub>2</sub>CO<sub>3</sub> was found to be the most effective and convenient base to use for the Heck reaction with palladium/zirconia catalyst (Table 5.3). The other reaction parameters have been optimized using K<sub>2</sub>CO<sub>3</sub> as a base. The organic bases triethylamine and tributylamine showed poorer performance in the Heck reaction.

**Table 5.3:** Results of arylation of acrylamide with 4-iodoanisole to afford 4-methoxycinnamicamide in the presence of different bases [reaction conditions = 2.5 mmol 4-iodoanisole + 6.5 mmol acrylamide + 7.23 mmol base + 5 ml DMF + catalyst (10 wt % of aryl halide), bath temperature 140 °C]

Base used	Reaction time (h)	Yield of 4-methoxy- <i>trans</i> -cinnamic amide (%)
NaOAc	15	25
Na <sub>2</sub> CO <sub>3</sub>	15	30
K <sub>2</sub> CO <sub>3</sub>	4	85
Zinc Dust	15	15
Pyridine	15	5
Et <sub>3</sub> N	15	7
Bu <sub>3</sub> N	15	6

### 5.3.7.2 Effect of Different Solvents

To check the efficiency of the catalyst and to optimize reaction conditions, different solvents have been used. The reaction between 4-iodoanisole with acryl amide was performed independently in toluene, xylene, acetonitrile, 1, 4-dioxan, NMP, DMF, ethanol and water as solvent (Table 5.4). DMF was found to be the best solvent for this reaction, which provided the product in quantitative yield.

**Table 5.4:** Results of arylation of acrylamide with 4-iodoanisole to afford 4-methoxycinnamicamide in the presence of different solvents [reaction conditions = 2.5 mmol 4-iodoanisole + 6.5 mmol acrylamide + 7.23 mmol  $K_2CO_3$  + 5 ml solvent + catalyst (10 wt % of aryl halide) and bath temperature 140 °C]

Solvent used	Reaction time (h)	Yield of 4-methoxy- <i>trans</i> -cinnamic amide (%)
DMF	4	85
H <sub>2</sub> O	10	No reaction
1,4 -Dioxan	12	No reaction
NMP	12	20
Xylene	12	5
Ethanol	12	No reaction
Toluene	12	No reaction

### 5.3.7.3 Effect of Reaction Temperature

The study of catalytic activity of Pd/zirconia catalyst in Heck reaction showed that the reactions can be performed at a lower temperature (at 110 °C), but the yield of product varies. In the case of aryl iodides and aryl bromides, the temperature close to reflux temperature (140

°C) is the best reaction temperature for the synthetic purpose. The inactivated and deactivated aryl halides require reaction temperature above 120 °C. To study the effect of temperature on the product yield, the reaction between 4-iodoanisole with acrylamide was performed at various temperatures and the results are shown in Table 5.5.

**Table 5.5:** Influence of temperature during arylation of acrylamide with 4-iodoanisole to 4-methoxycinnamicamide [reaction conditions = 2.5 mmol 4-iodoanisole + 6.5 mmol acrylamide + 7.23 mmol K<sub>2</sub>CO<sub>3</sub> + 5 ml DMF + catalyst (10 wt % of aryl halide)]

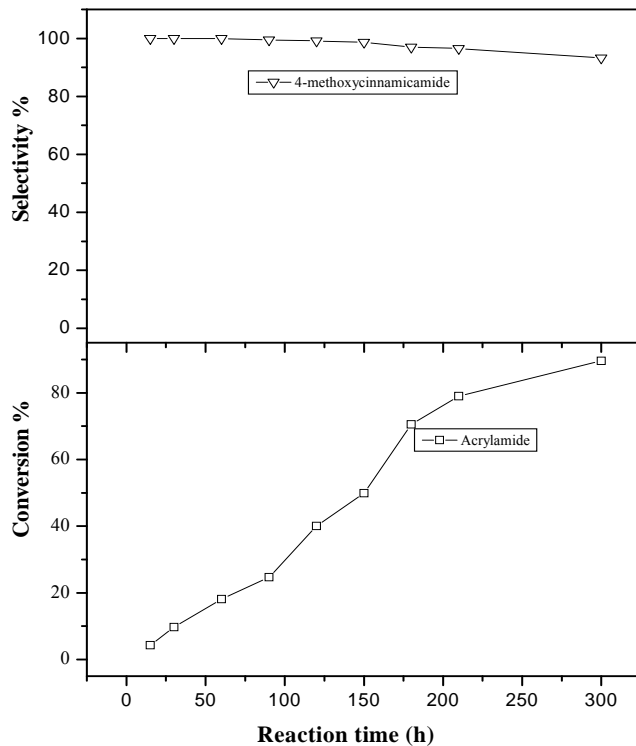
Bath temperature (°C)	Reaction Time (h)	Yield (%)
0	20	No reaction
50	20	No reaction
100	10	41.5
140	4	85

As it can be seen here that as the temperature of the reaction increases, the product yield also increases with decrease in reaction period. No reaction occurred at 0 °C and 50 °C, however, only 41.5 % yield was obtained at 100 °C. The highest product yield was obtained at the temperature of 140 °C.

#### 5.3.7.4 Effect of Reaction Time

The results showing the influence of reaction time for the reaction of acrylamide with 4-iodoanisole to 4-methoxycinnamicamide at 140 °C over the Pd/ZrO<sub>2</sub> catalyst are presented in Figure 5.3. The conversion of acrylamide and selectivity for 4-methoxycinnamicamide

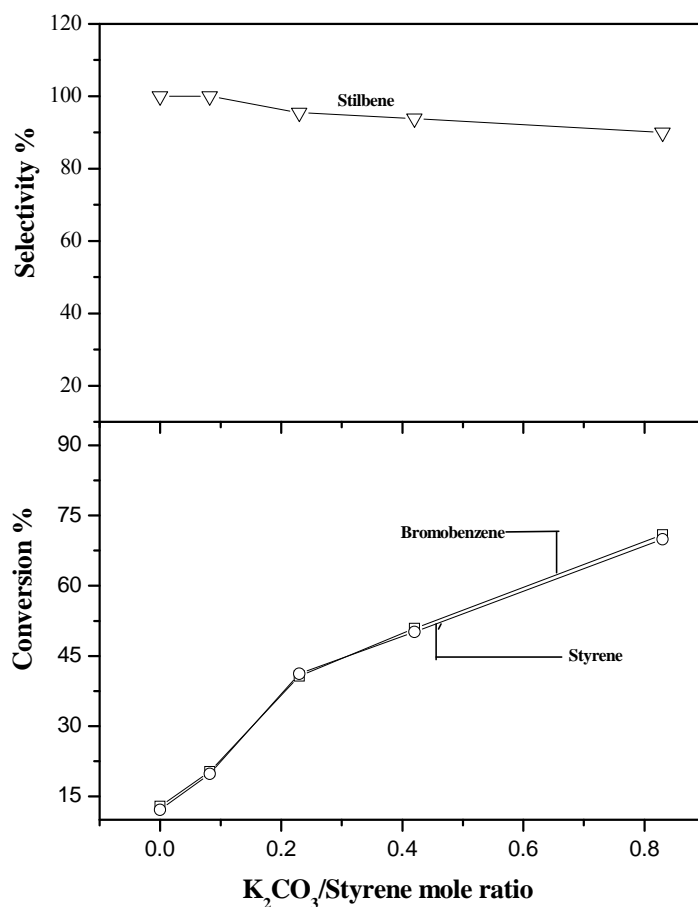
increased almost linearly with increasing the reaction time. The product selectivity, however, decreased slightly with the time.



**Figure 5.3:** Effect of the reaction time on the conversion of acrylamide and selectivity for 4-methoxycinnamicamide in the arylation of acrylamide with 4-iodoanisole [reaction conditions = 2.5 mmol 4-iodoanisole + 6.5 mmol acrylamide + 7.23 mmol  $K_2CO_3$  + 5 ml DMF + catalyst (10 wt % of aryl halide) and bath temperature 140 °C]

#### 5.3.7.5 Effect of $K_2CO_3$ /styrene Mole Ratio

The results showing the influence of base  $K_2CO_3$ /styrene mole ratio on the conversion of bromobenzene and styrene and selectivity for stilbene over palladium/zirconia (impregnation) catalyst are presented in Figure 5.4.



**Figure 5.4:** Influence of the base  $K_2CO_3$ /styrene mole ratio on the conversion and stilbene selectivity in the arylation of styrene by bromobenzene over Pd/zirconia [reaction conditions = 2.5 mmol bromobenzene + 6.5 mmol styrene + 5 ml DMF +  $K_2CO_3$  + catalyst (10 wt % of aryl halide) and bath temperature 140 °C]

The conversion increased markedly while product selectivity decreased significantly with the increase in the concentration of  $K_2CO_3$  relative to that of styrene in the reaction mixture.

### 5.3.7.6 Reusability Test of the Catalyst

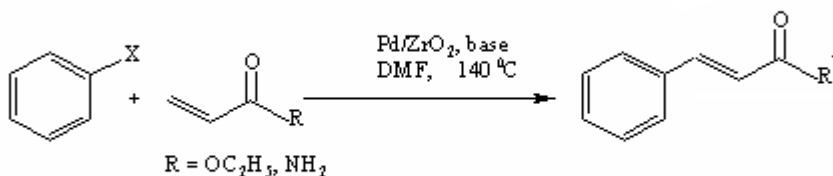
In order to test the catalyst reusability, the palladium/zirconia catalyst was removed from the reaction mixture simply by filtration, washed with DMF first and then with acetone, dried and reused in the arylation of acrylamide with 4-iodoanisole at 140 °C. This was repeated several times. The results showing the reusability of the catalyst are presented in Table 5.6. It is interesting to note that the catalyst showed excellent reusability without significant decrease in the yield. The observed increase in the reaction period for completing the reaction is expected because of the decrease in the recovered catalyst (which is expected due to filtration loss).

**Table 5.6:** Reuse of the palladium/zirconia catalyst in the arylation of acrylamide with 4-iodoanisole [reaction conditions = 2.5 mmol 4-iodoanisole + 6.5 mmol acrylamide + 7.23 mmol K<sub>2</sub>CO<sub>3</sub> + 5 ml DMF + catalyst and bath temperature 140 °C]

Reuse of Catalyst	Reaction Time (h)	Product Yield (%)
Reuse I	5	85
Reuse II	6	85
Reuse III	7	84
Reuse IV	8.5	83

### 5.3.8 Preparation of Substituted Styrenes and Substituted *trans*-Stilbenes

#### 5.3.8.1 Preparation of Substituted Styrenes by the Heck reaction in presence of Pd/ZrO<sub>2</sub>



Scheme 5.2

When various aryl halides were reacted with acrylate, acrylamide and acrylonitrile in dimethyl formamide in presence of palladium on zirconia catalyst (10 wt. % of aryl halide) (Scheme 5.2), the corresponding substituted styrenes were obtained in good yields (Table 5.7). A number of substituted styrenes were prepared to generalize the method. The encouraging results obtained in the preparation of substituted styrenes were explored further to synthesize substituted stilbenes (described later).

#### *General Procedure for the preparation of substituted styrenes by the Heck reaction in presence of Pd/zirconia catalyst*

To 5 ml of DMF, were added 2.5 mmol of aryl halide, 6.5 mmol of alkene, catalyst (10 wt % of aryl halide) and 7.23 mmol K<sub>2</sub>CO<sub>3</sub>. The mixture was stirred at a bath temperature of 140 °C in nitrogen atmosphere for an appropriate time and the reaction was monitored by TLC. After completion of reaction, the catalyst was separated by filtration and washed with DMF (3 x 3 ml). Then the filtrate was quenched with water followed by extraction with ethyl acetate to give the crude product, which was subsequently purified by column chromatography on silica gel with petroleum ether/ethyl acetate as eluent. The catalyst was further washed with acetone,



dried and reused. The reaction products were isolated by column chromatography and were characterized by NMR, IR, MS spectroscopy and elemental analysis.

Using the above procedure, following substituted styrenes were prepared:

**Table 5.7:** Preparation of Substituted Styrenes

Sr no	Substrates used		Time (h)	Product <sup>a</sup>	Yield (%)
	Aryl halide	Olefin			
1	<i>p</i> -Iodoanisole	Acrylamide	4	4-Methoxy- <i>trans</i> -cinnamic amide	85
2	<i>p</i> -Iodoanisole	Methyl acrylate	4	Methyl 4-methoxy- <i>trans</i> -cinnamate	75
3	<i>p</i> -Iodoanisole	Acrylonitrile	3.5	4-Methoxy-cinnamionitrile	70
4	4-Bromoacetophenone	Methyl acrylate	5	Methyl 4-acetyl - <i>trans</i> -cinnamate	75
5	<i>p</i> -Iodoanisole	Methyl 3-(4-methoxyphenyl)-acrylate	6	Methyl 3,3-bis-(4-methoxyphenyl)-Acrylate	70

<sup>a</sup>The products were characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR and mass spectroscopy

The spectral data of some of the substituted styrenes are shown below

**4-Methoxy- *trans* -cinnamic amide (1)**<sup>42</sup>

Off-white powder; mp 199-200 °C; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 75 MHz): δ 7.33 (d, J=8 Hz, 2H), 7.29 (br s, 1H), 7.20 (d, J=15 Hz, 1H), 6.84 (br s, 1H), 6.80 (d, J=8 Hz, 2H), 6.30 (d, J=15 Hz, 1H), 3.61 (s, 3H); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>, 75 MHz): δ 167.3, 160.5, 139.1, 129.2 (2C), 127.6, 119.9, 114.5 (2C), 55.4; Mass (+TOF): 178.11 [M+1], 200.04 [M+Na]; Anal Calcd for C<sub>10</sub>H<sub>11</sub>O<sub>2</sub>N :

C, 67.78; H, 6.20; N, 7.90% ; Found: C, 67.70; H, 6.24; N, 7.80; IR (chloroform): 3461, 3358, 3020, 1662, 1602, 1513, 1425  $\text{cm}^{-1}$ .

***Methyl 4-methoxy- trans- cinnamate (2)***<sup>43</sup>

White solid; mp 86-87 °C; <sup>1</sup>H NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  7.64 (d, J=15 Hz, 1H), 7.47 (d, J=9 Hz, 2H), 6.89 (d, J=9 Hz, 2H), 6.30 (d, J=15 Hz, 1H), 3.84 (s, 3H), 3.79 (s, 3H); <sup>13</sup>C NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz ):  $\delta$  167.3, 161.2, 144.3, 129.6 (2C), 127.0, 115.2, 114.2 (2C), 55.0, 51.3; Mass (+TOF): 192.78 [ $\text{M}^+$ ], 214.67 [ $\text{M}+\text{Na}$ ]; IR (chloroform): 2963, 1714, 1635, 1604, 1513, 1330, 1288, 1256, 1174, 1026, 984, 836, 755  $\text{cm}^{-1}$ .

***4-Methoxy cinnamotrile (3)***<sup>44</sup>

Faint yellow semisolid; <sup>1</sup>H NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz) for (E) isomer:  $\delta$  7.27 (d, J=9 Hz, 2H), 7.19 (d, J=16 Hz, 1H), 6.80 (d, J=9 Hz, 2H), 5.59 (d, J=16 Hz, 1H), 3.73 (s, 3H); <sup>1</sup>H NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz) for (Z) isomer:  $\delta$  7.67 (d, J=9 Hz, 2H), 6.92 (d, J=12 Hz, 1H), 6.81 (d, J=9 Hz, 2H), 5.17 (d, J=12 Hz, 1H), 3.73 (s, 3H); Anal Calcd for  $\text{C}_{10}\text{H}_9\text{ON}$  : C, 75.46; H, 5.69; N, 8.79%; Found: C, 75.48; H, 5.60; N, 8.74%; IR (chloroform): 2213  $\text{cm}^{-1}$ .

***Methyl 4-acetyl- trans- cinnamate (4)***<sup>45</sup>

Off-white solid; mp 104 °C; <sup>1</sup>H NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  7.97 (d, J=9 Hz, 2H), 7.70 (d, J=16 Hz, 1H), 7.61 (d, J=9 Hz, 2H), 6.52 (d, J=16 Hz, 1H), 3.83 (s, 3H), 2.62 (s, 3H); <sup>13</sup>C NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  196.3, 166.2, 142.7, 138.2, 137.6, 128.4 (2C), 127.7(2C), 119.9, 51.3, 26.1; Anal. Calcd for  $\text{C}_{12}\text{H}_{12}\text{O}_3$ : C, 70.57; H, 5.92 %; Found: C, 70.47; H, 5.80%; IR (chloroform): 3020, 1717, 1684, 1266, 758  $\text{cm}^{-1}$ .

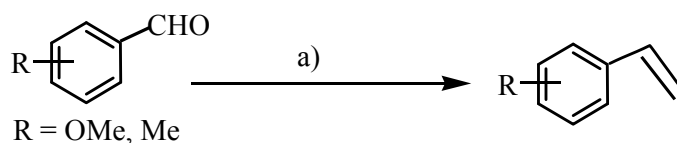
***Methyl 3, 3-bis-(4-methoxyphenyl)-acrylate (5)***<sup>43</sup>

Semisolid; <sup>1</sup>H NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  7.29 (d, J=9 Hz, 2H), 7.20 (d, J=9 Hz, 2H), 6.96 (d, J=9 Hz, 2H), 6.88 (d, J=9 Hz, 2H), 6.27 (s, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.68 (s, 3H); <sup>13</sup>C NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 75 MHz):  $\delta$  165.9, 160.3, 159.2, 156.1, 133.4, 130.6, 130.4 (2C),

129.4 (2C), 113.8, 113.2 (2C), 112.7 (2C), 54.6, 54.5, 50.3; Anal. Calcd for C<sub>18</sub>H<sub>18</sub>O<sub>4</sub>: C, 72.48; H, 6.04 %; Found: C, 72.40; H, 6.00%; IR (chloroform): 3019, 1710, 1633, 1512, 1249, 116 cm<sup>-1</sup>.

### 5.3.8.2 Preparation of Substituted Styrenes (used as starting materials for the Heck Reaction) by Wittig reaction

The substituted styrenes, which were used as starting materials for Heck reaction catalyzed by pd/zirconia, were prepared by a Wittig reaction method as follows:



**Scheme 5.3**

a) Ph<sub>3</sub>P<sup>+</sup>-Me-Br<sup>-</sup>, THF, -78 °C, nBuLi

The Ph<sub>3</sub>P<sup>+</sup>-Me-Br<sup>-</sup> (1.2 equiv., 10.9 g, 30 mmol) was taken in two neck round bottom flask, dry tetrahydrofuran (100 ml) was added under nitrogen atmosphere, stirred for five minutes, n-butyllithium (1.2 equiv., 2.88 ml, 30.5 mmol) was added drop wise at -78 °C (dry ice + acetone) over 15 minutes and the reaction mixture was stirred at 25 °C for 3 h. Then the substituted benzaldehyde (1 equiv. 5 g, 25.5 mmol) in tetrahydrofuran (50 ml) was added drop wise and stirred at 25 °C for 20 minutes. Then the reaction mixture was heated at 60 °C for 10 h and the reaction was monitored by TLC. After completion of reaction, the reaction mixture was quenched with methanol and the mixture was allowed to cool to room temperature.

Methanol was removed under reduced pressure and the residue was extracted with ethyl acetate. The organic layer was washed with water followed by brine, dried over sodium sulfate and concentrated to dryness under reduced pressure using rotary evaporator. The crude residue was purified by column chromatography using silica gel (petroleum ether/ethyl acetate as an eluent) to collect the pure product, which was characterized, by NMR, IR and Mass spectroscopy and elemental analysis.

The substituted styrenes thus prepared and used as starting materials, subjected to the Heck reaction with aryl halides as presented in Table 5.6 to afford the desired *trans*-stilbenes in good yields.

The spectral data of some of the substituted styrenes are shown below

**3, 4, 5-Trimethoxystyrene (6)**

$^1\text{H}$  NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  6.55-6.70 (m, 3H), 5.64 (d,  $J = 16$  Hz, 1H), 5.21 (d,  $J = 12$  Hz, 1H), 3.89 (s, 6 Hz), 3.85 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  153.3 (2C), 138.13, 136.8, 133.2, 113.1, 103.4 (2C), 60.76, 55.98 (2C); IR (chloroform): 3395, 3019, 1694, 1583, 1215, 1131, 758  $\text{cm}^{-1}$ ; GCMS:  $m/z$  194.

**4-Methoxystyrene (7)**

$^1\text{H}$  NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  7.38 (d,  $J = 8$  Hz, 2H), 6.89 (d,  $J = 10$  Hz, 2H), 6.71 (dd,  $J = 10$  Hz, 18 Hz, 1H), 5.65 (d,  $J = 18$  Hz, 1H), 5.17 (d,  $J = 12$  Hz, 1H), 3.84 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3 + \text{CCl}_4$ , 50 MHz):  $\delta$  159.4, 136.3, 130.5, 127.4 (2C), 113.9 (2C), 111.5, 55.2.

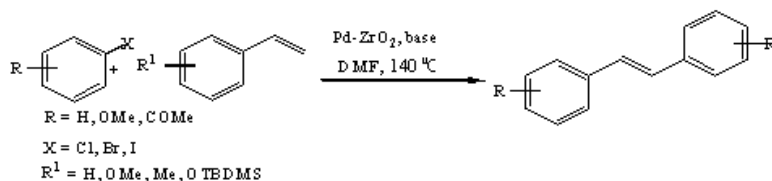
**3, 5-Dimethoxystyrene (8)**

$^1\text{H}$  NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  6.66 (dd,  $J = 10$  Hz, 16 Hz, 1H), 6.56 (d,  $J = 2$  Hz, 2H), 6.39 (t,  $J = 6$  Hz, 1H), 5.73 (d,  $J = 16$  Hz, 1H), 5.27 (d,  $J = 10$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  160.9 (2C), 139.6, 136.9, 114.2, 104.4 (2C), 100.1, 55.2 (2C); IR (chloroform): 3006, 2939, 1831, 1593, 1458, 1315, 1205, 1156  $\text{cm}^{-1}$ ; GCMS:  $m/z$  164.

### 3, 4-Dimethylstyrene (9)

$^1\text{H}$  NMR ( $\text{CDCl}_3 + \text{CCl}_4$ , 50 MHz):  $\delta$  7.10-7.30 (m, 3H), 6.69 (dd,  $J = 10$  Hz, 16 Hz, 1H), 5.71 (d,  $J = 18$  Hz, 1H), 5.19 (d,  $J = 12$  Hz, 1H), 2.30 (s, 6H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3 + \text{CCl}_4$ , 50 MHz):  $\delta$  136.4 (2C), 136.8, 135.3, 129.8, 127.5, 123.7, 112.5, 19.8, 19.6.

#### 5.3.8.3 Preparation of Substituted Stilbenes by the Heck reaction in presence of Pd/zirconia

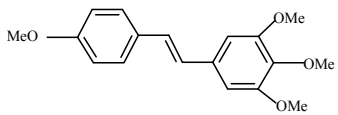
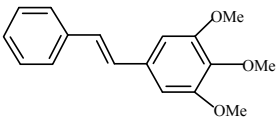
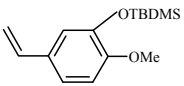
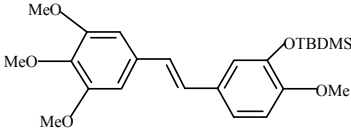
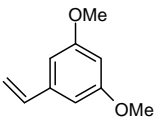
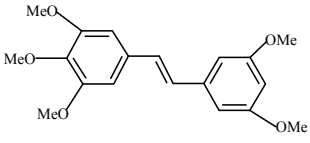
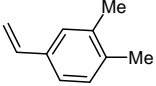
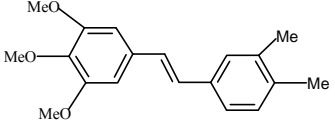


Scheme 5.4

The styrenes were prepared by Wittig method as discussed in Sec. 5.3.8.2, and subjected to Heck reaction with aryl halide in presence of palladium/zirconia catalyst to give substituted stilbenes as Scheme 5.4. The general procedure for the preparation of substituted stilbenes by the Heck reaction in presence of pd/zirconia catalyst is already discussed in Sec.5.3.8.1 as per the preparation of substituted styrenes. The encouraging results obtained in the preparation of substituted *trans*-stilbenes, which exhibits a wide variety of biological activity as shown in Table 5.8.

The catalytic activity, as expected, depends on the substituents on the aryl halide and olefin. The compounds, which contain electron-withdrawing groups on the aryl ring, increased the rate of reaction. Bromobenzene, a relatively inactive halide, gave low yield of *trans*-stilbene after reaction with styrene at the time interval of 12 h, iodobenzene gave excellent yield whereas chlorobenzene gave  $\leq 5$  % yield.

**Table 5.8:** Preparation of Substituted Stilbenes

Sr. no	Substrates used		Time (h)	Product <sup>a</sup>	Yield (%)
	Aryl halide	Olefin			
1	Iodobenzene	Styrene	7	<i>trans</i> -Stilbene	83
2	Bromobenzene	Styrene	15	<i>trans</i> -Stilbene	66
3	Chlorobenzene	Styrene	30	<i>trans</i> -Stilbene	≤5
4	3-Bromoacetophenone	Styrene	9	3-Acetyl- <i>trans</i> -stilbene	65
5	4-Bromoacetophenone	Styrene	7	4-Acetyl- <i>trans</i> -stilbene	68
6	<i>p</i> -Iodoanisole	Styrene	4	4-Methoxy- <i>trans</i> -stilbene	71
7	<i>p</i> -Iodoanisole	4-Methoxystyrene	5	4,4'-Dimethoxy- <i>trans</i> -stilbene	85
8	<i>p</i> -Iodoanisole	3,5-Dimethoxystyrene	5	3,4',5-Trimethoxy- <i>trans</i> -stilbene	69
9	<i>p</i> -Iodoanisole	3,4,5-Trimethoxystyrene	4		70
10	3,4,5-Trimethoxyiodobenzene	Styrene	7		70
11	3,4,5-Trimethoxyiodobenzene		7		80
12	3,4,5-Trimethoxyiodobenzene		7		75
13	3,4,5-Trimethoxyiodobenzene		5		45

<sup>a</sup>The products were characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR and mass spectroscopy

Iodobenzenes substituted with electron withdrawing or electron-donating groups also gave excellent yield, without addition of any additives. The styrenes with electron withdrawing

as well as electron donating groups also reacted well and gave quantitative yield with aryl iodides and bromides. The reactions of iodoarenes containing electron withdrawing or electron-donating groups with ethyl acrylates, styrenes were performed under the optimized conditions. All the coupling reactions proceeded smoothly to give the corresponding (*E*)-cinnamates and stilbenes in good to excellent yield.

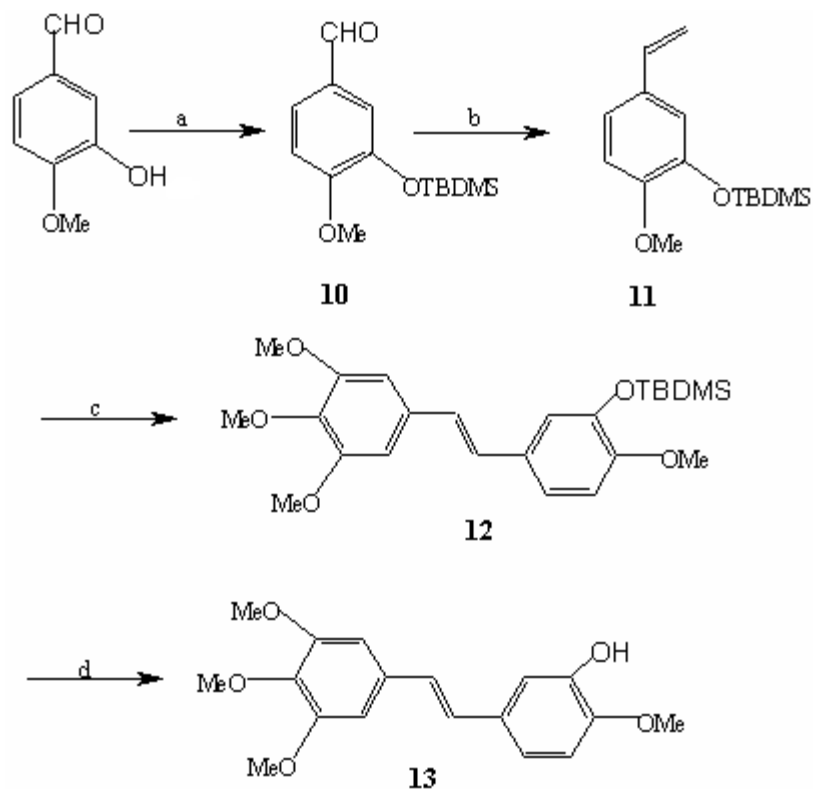
The encouraging results obtained in the preparation of substituted *trans*-stilbenes, which exhibit a wide variety of biological activity; therefore this methodology was applied for the preparation of *trans* combretastatin A-4. The synthetic sequence followed is shown in Scheme 5.5.

#### **5.3.8.4: Preparation of *trans*-Combretastatin A-4 [*trans*-1(3-Hydroxy-4-methoxyphenyl)-2-(3,4,5-trimethoxyphenyl) ethene] using Heck Reaction Approach**

The heterogeneous Pd/zirconia catalyst was used to prepare the anticancer compound *trans*-combretastatin A-4. The synthetic sequence for the above mentioned compound by applying the Heck reaction approach is shown in Scheme 5.5. The Heck reaction was performed at 140 °C, and the product obtained was found to possess the *trans* geometry.

##### **5.3.8.4.1 Preparation of *tert*-butyldimethylsilyl derivative 10**

A solution of 3-hydroxy-4-methoxy benzaldehyde (2 g, 13.2 mmol) in dry dichloromethane (5 ml) was stirred at 0 °C under inert atmosphere (maintained by using nitrogen gas filled in balloon), a solution of *tert*-butyldimethylsilylchloride (1.2 eq., 12.5 mmol) and dimethylaminopyridine (10 % w.r.t.starting material) in dichloromethane (5 ml) was added drop wise and stirred at same temperature for 15 min. Then triethylamine (2 eq., 3.5 ml) was added and mixture was warmed to room temperature and stirred further for 3 h (monitored by TLC). The reaction mixture was filtered through Whatman filter paper, dichloromethane was



- a) TBDMSCl, DMAP, DCM, Et<sub>3</sub>N, 5h, 91 %  
 b) Ph<sub>3</sub>P<sup>+</sup>-Me-Br THF, -78 °C, nBuLi, 85 %  
 c) 3,4,5-trimethoxy-iodobenzene, Pd/ZrO<sub>2</sub> cat.(10 % w.r.t.aryl halide),  
 K<sub>2</sub>CO<sub>3</sub>, DMF,140 °C, 7h, 80 %,   
 d) CH<sub>3</sub>COOH-THF-H<sub>2</sub>O(3:1:1), 50 °C, 20h, 55 %.

**Scheme 5.5**

removed under reduced pressure and extracted with chloroform. The organic layer was washed with water followed by brine, dried over sodium sulfate and concentrated to dryness under reduced pressure using rotary evaporator. The crude residue was purified by column chromatography using silica gel (petroleum ether/ethyl acetate as an eluent) to give the title derivative **10** (1.6 g, 91 %).

The intermediate **11** was prepared by Wittig method and the procedure is already discussed in section 5.3.8.2.



### ***3-tert-Butyldimethylsilanyloxy-4-methoxystyrene (11)***

$^1\text{H}$  NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  6.73-6.79 (m, 2H), 6.60 (d,  $J = 10$  Hz, 1H), 6.42 (dd,  $J = 10$  Hz, 18 Hz, 1H), 5.39 (d,  $J = 16$  Hz), 4.93 (d,  $J = 10$  Hz, 1H), 3.63 (s, 3H), 0.85 (s, 9H), 0.00 (s, 6H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  190.2, 156.2, 145.3, 129.9, 125.9, 119.6, 110.8, 55.2, 25.4 (3C), 18.2, 4.9 (2C); IR (chloroform): 3396, 2931, 2858, 1685, 1595, 1508, 1442, 1281, 1216, 1133, 850  $\text{cm}^{-1}$ .

#### ***5.3.8.4.2 Preparation of trans-1- (3-tert-butyldimethylsilanyloxy-4-methoxyphenyl)-2-(3,4,5-trimethoxyphenyl)- ethene 12 (Heck Reaction)***

To intermediate **11** and a commercially available 3, 4, 5-trimethoxy-iodobenzene (2.5 mmol) in DMF (5 ml) were added Pd/zirconia catalyst (10 wt % w.r.t. aryl halide) and  $\text{K}_2\text{CO}_3$  (7.23 mmol). The mixture was stirred at a bath temperature of 140 °C in nitrogen atmosphere for an appropriate time and the reaction was monitored by TLC. After completion of reaction, the catalyst was separated by filtration and washed with DMF (3 x 3 ml). Then the filtrate was diluted with water followed by extraction with ethyl acetate to give the crude product, which was subsequently purified by column chromatography on silica gel with petroleum ether/ethyl acetate as an eluent to get compound **12** (80 %). The catalyst was further washed with acetone, dried and reused. The reaction products were isolated by column chromatography and were confirmed by NMR, IR and Mass spectroscopy and elemental analysis.

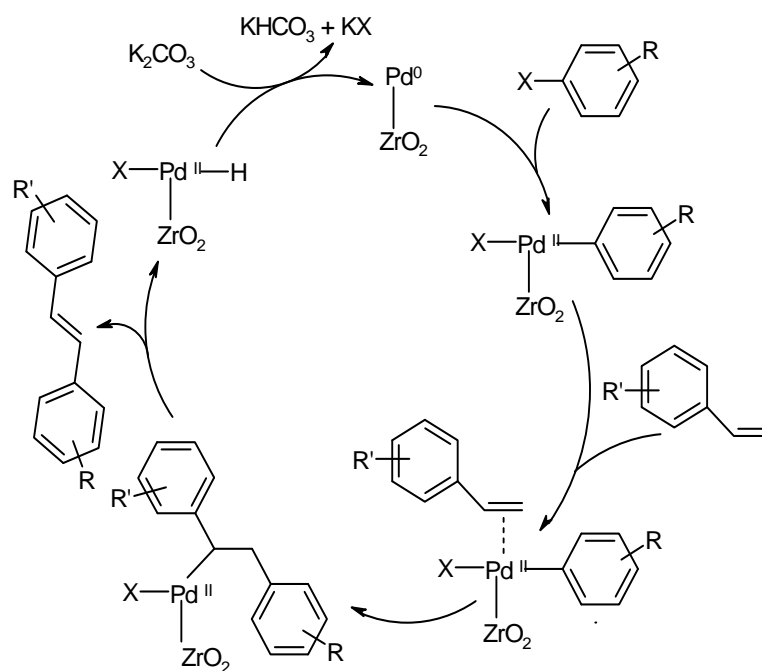
Faint yellowish semisolid,  $^1\text{H}$  NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  7.07-6.79 (m, 5H), 6.70 (s, 2H), 3.92 (s, 6H), 3.86 (s, 3H), 3.83 (s, 3H), 1.04 (s, 9H), 0.19 (s, 6H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 100 MHz): 153.4 (2C), 150.8, 145.2, 137.8, 133.4, 130.5, 127.9, 126.7, 120.5, 118.6, 112.0, 103.4 (2C), 60.9, 56.1 (2C), 55.4, 25.8 (3C), 18.5, 4.5 (2C).

**5.3.8.4.3 Preparation of *trans*-1-(3-hydroxy-4-methoxyphenyl)-2-(3, 4, 5-trimethoxy-phenyl)-ethene [*trans*-Combretastatin A-4] **13****

In a 50 ml round bottom flask, *trans*-1-(3-tertbutyldimethylsilyloxy-4-methoxyphenyl)-2-(3, 4, 5-trimethoxyphenyl)-ethene **12** was taken in a mixture of acetic acid, tetrahydrofuran and water (3:1:1) (20 ml) and the mixture was heated at 50 °C for 20 h (monitored by TLC). The reaction mixture was cooled to 0 °C and neutralized by adding sodium bicarbonate and then extracted with chloroform (3 x 20 ml). The organic layer was washed with water followed by brine and dried over sodium sulfate and solvent was removed under reduced pressure using rotary evaporator. The crude residue was purified by column chromatography using silica gel (petroleum ether/ethyl acetate as an eluent) to collect the pure compound **13** (0.03 g, 55 %) as off-white solid.

Mp: 104 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 50 MHz): δ 7.12 (d, J=2 Hz, 1H), 6.95 (dd, J=8 Hz, 2H, 1H), 6.91 (d, J=16 Hz, 1H), 6.84 (d, J=16 Hz, 1H), 6.82 (d, J=8 Hz, 1H), 6.69 (s, 2H), 3.92 (s, 9H), 3.86 (s, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 100 MHz): 153.1 (2C), 146.1, 145.6, 137.5, 133.0, 130.8, 127.5, 126.8, 118.8, 111.5, 110.3, 103.2(2C), 60.6, 55.7 (2C), 55.6; Mass (+TOF): 317.565[M+1], 339.581 [M+Na]; Anal. Calcd for C<sub>18</sub>H<sub>20</sub>O<sub>5</sub>: C, 68.35; H, 6.32%; Found: C, 68.30; H, 6.39%.

The possible mechanism of Heck arylation of aryl halide over supported palladium catalysts is shown in Scheme 5.6. In the first step, catalytically active Pd complexes [Pd/zirconia-(solvent)-(base)] are formed by the coordination of polar solvents and base. The oxidative addition of aryl halide to the catalyst forms an intermediate [Ph-Pd/zirconia-(solvent)



**Scheme 5.6**

-(base)]. Then followed by insertion of olefin to an intermediate species. The syn elimination of [H-Pd/zirconia-(solvent)-(base)] from the intermediate species formed the desired *trans*-product, followed by reductive elimination of base. The active Pd species is generated back.

#### 5.4 CONCLUSIONS

In conclusion, we have demonstrated that palladium on zirconia catalyst is useful for the synthesis of various styrenes and biological active *trans*-stilbenes. The reaction conditions are amenable to scale up making the present method suitable to make available the substituted stilbenes in larger quantities for detailed biological activity studies. Also, the present work employs a heterogeneous catalyst that is easily removed from the product simply by filtration and can be recovered and reused as a highly efficient catalyst for the Heck reaction.

The spectral data of some Heck reaction products are shown below.

### Spectral data

#### ***trans*-stilbene (14)**<sup>43, 46</sup>

White crystalline solid; mp 123 °C, <sup>1</sup>H NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 50 MHz): δ 7.57 (d, J=8 Hz, 4H), 7.47- 7.25 (m, 6H), 7.16 (s, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 50 MHz): δ 137.3 (2C), 128.7 (4C), 127.6 (2C), 126.5 (4C); IR (chloroform,): 3019, 1600, 1497, 1452, 961, 758 cm<sup>-1</sup>.

#### **4-Acetyl-*trans*-stilbene (15)**<sup>46, 47</sup>

White solid; mp 131 °C, <sup>1</sup>H NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 50 MHz): δ 8.02 (d, J=9 Hz, 2H), 7.66 (d, J=9 Hz, 2H), 7.61(d, J=9 Hz, 2H), 7.51-7.32 (m, 3H), 7.26 (d, J=15 Hz, 1H), 7.19 (d, J=15 Hz, 1H), 2.69 (s, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 50 MHz): δ 196.9, 141.9, 136.7, 135.9, 131.4, 128.8 (2C), 128.7 (2C), 128.3, 127.4, 126.7 (2C), 126.4 (2C), 26.4; Mass (+TOF):223.872 [M+1], 245.810 [M+Na]; Anal. Calcd for C<sub>16</sub>H<sub>14</sub>O: C, 86.45; H, 6.34 %; Found: C, 86.53; H, 6.30%; IR (chloroform): 3019, 1676, 1601, 1267, 964, 755 cm<sup>-1</sup>.

#### **3-Acetyl-*trans*- stilbene (16)**<sup>48</sup>

Off- white solid; mp 78 °C, <sup>1</sup>H NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 50 MHz): δ 8.05 (t, J=2 Hz, 1H), 7.83-7.62 (m, 2H), 7.52-7.20 (m, 6H), 7.16 (d, J=16 Hz, 1H), 7.07 (d, J=16 Hz, 1H), 2.60 (s, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 100 MHz): δ 197.7, 137.9, 137.6, 136.9, 130.8, 130.0, 128.9, 128.7 (2C), 128.0, 127.5, 127.4, 126.6 (2C), 126.2, 26.6; Mass (+TOF): 223.872 [M+1], 245.810 [M+Na]; Anal. Calcd for C<sub>16</sub>H<sub>14</sub>O: C, 86.45; H, 6.34 %; Found: C, 86.53; H, 6.30%; IR (chloroform): 3019, 1678, 1602, 1560, 1360, 1267, 963, 757 cm<sup>-1</sup>.

#### **4-Methoxy- *trans*- stilbene (17)**<sup>46</sup>

Off- white solid; mp 137 °C, <sup>1</sup>H NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 50 MHz): δ 7.57-7.46 (m, 4H), 7.39 (t, J=8 Hz, 2H), 7.31-7.22 (m, 1H), 7.12 (d, J=16 Hz, 1H), 7.00 (d, J=16 Hz, 1H), 6.94 (d, J=8 Hz, 2H), 3.89 (s, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 100 MHz): 159.4, 137.8, 130.3, 128.7(2C), 128.3, 127.7 (2C), 127.2, 126.7, 126.3 (2C), 114.2 (2C), 55.2; GCMS: 210; Anal. Calcd for C<sub>15</sub>H<sub>14</sub>O:

C, 85.68; H, 6.71%; Found: C, 85.57; H, 6.70%; IR (chloroform): 3019, 1602, 1512, 929, 758  $\text{cm}^{-1}$ .

***trans*-1-phenyl-2-(3,4,5-trimethoxyphenyl) ethene (18)** <sup>49</sup>

White solid; mp 105°C, <sup>1</sup>H NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  7.45-7.38 (m, 2H), 7.32-7.15 (m, 3H), 6.96 (d, J=16 Hz, 1H), 7.88 (d, J=16 Hz, 1H), 6.64 (s, 2H), 3.84 (s, 6H), 3.79 (s, 3H); <sup>13</sup>C NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 100 MHz): 153.4 (2C), 138.2, 137.2, 133.1, 128.8, 128.7 (2C), 128.2, 127.6, 126.4 (2C), 103.8 (2C), 60.9, 56.1 (2C); Mass (+TOF): 271.739 [M+1], 293.765 [M+Na]; Anal. Calcd for  $\text{C}_{17}\text{H}_{18}\text{O}_3$ : C, 75.55; H, 6.66%; Found C, 75.44; H, 6.62%; IR (chloroform): 3019, 1584, 1420, 758  $\text{cm}^{-1}$ .

***trans*-1-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenyl)-ethene (19)** <sup>49</sup>

White solid; mp 154 °C, <sup>1</sup>H NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  7.43 (d, J=9 Hz, 2H), 6.97 (d, J=16 Hz, 1H), 6.89 (d, J=9 Hz, 2H), 6.87 (d, J=16 Hz, 1H), 6.70 (s, 2H), 3.93 (s, 6H), 3.87 (s, 3H), 3.84 (s, 3H); <sup>13</sup>C NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 100 MHz): 159.4, 153.5 (2C), 137.9, 133.5, 130.1, 127.8, 127.7 (2C), 126.7, 114.2 (2C), 103.6 (2C), 60.9, 56.2 (2C), 55.3; Mass (+TOF): 301.581 [M+1], 323.590 [M+Na]; Anal. Calcd for  $\text{C}_{18}\text{H}_{20}\text{O}_4$ : C, 72; H, 6.66%; Found: C, 71.8; H, 6.60%; IR (chloroform): 3019, 1599, 1578, 1496, 1451, 961  $\text{cm}^{-1}$ .

**4, 4'-Dimethoxy- *trans*- stilbene (20)** <sup>50</sup>

White solid; mp 210 °C; <sup>1</sup>H NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  7.41 (d, J=10 Hz, 4H), 6.92 (s, 2H), 6.87 (d, J=10 Hz, 4H), 3.84 (s, 6H); <sup>13</sup>C NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 100 MHz): 159.0 (2C), 130.5 (2C), 127.4 (4C), 126.2 (2C), 114.1 (4C), 55.2 (2C); Mass (+TOF): 241.697[M+1], 263.546 [M+Na]; Anal. Calcd for  $\text{C}_{16}\text{H}_{16}\text{O}_2$ : C, 80.0; H, 6.66 %; Found: C, 80.0; H, 6.60%; IR (chloroform): 3020, 1665, 1608, 1514  $\text{cm}^{-1}$ .

**3, 4', 5-Trimethoxy- *trans*- stilbene (21)** <sup>51</sup>

White solid; mp: 57 °C; <sup>1</sup>H NMR ( $\text{CDCl}_3+\text{CCl}_4$ , 50 MHz):  $\delta$  7.44 (d, J=8 Hz, 2H), 7.04 (d, J=16 Hz, 1H), 6.90 (d, J=16 Hz, 1H), 6.89 (d, J=8 Hz, 2H), 6.63 (d, J=2 Hz, 2H), 6.36 (t, J=2 Hz,

1H), 3.84 (s, 9H); <sup>13</sup>C NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 100 MHz): 161.0 (2C), 159.4, 139.7, 130.0, 128.7, 127.8 (2C), 126.7, 114.1 (2C), 104.4 (2C), 99.7, 55.2 (3C); Mass (+TOF): 271.409 [M+1], 293.426 [M+Na]; Anal. Calcd for C<sub>17</sub>H<sub>18</sub>O<sub>3</sub>: C, 75.56; H, 6.67%; Found: C, 75.55; H, 6.71%; IR (chloroform): 3019, 1599, 758 cm<sup>-1</sup>.

***trans*-1-(3, 5-Dimethoxyphenyl)-2-(3, 4, 5-trimethoxyphenyl)-ethene (22)**<sup>51</sup>

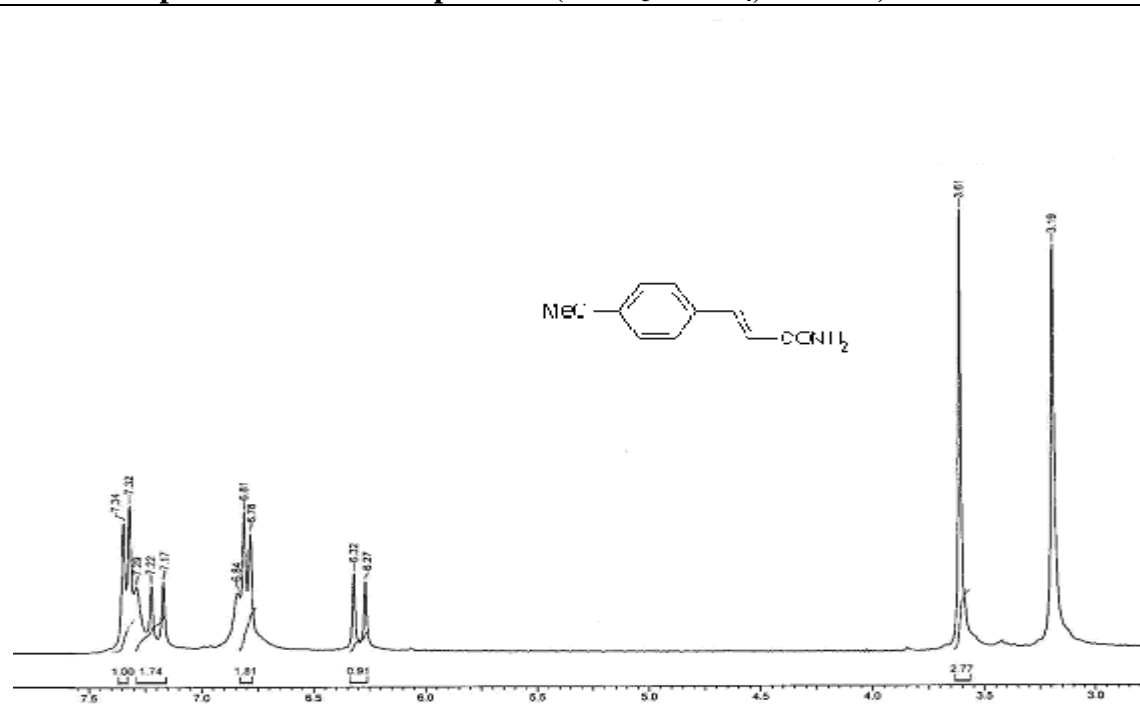
White solid; mp: 138 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 50 MHz): δ 7.01 (d, J=16 Hz, 1H), 6.90 (d, J=16 Hz, 1H), 6.72 (s, 2H), 6.65 (d, J=2 Hz, 2H), 6.38 (t, J=2 Hz, 1H), 3.93 (s, 6H), 3.87 (s, 3H), 3.84 (s, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 100 MHz): 161.1 (2C), 153.5 (2C), 139.2, 132.9 (2C), 129.2, 128.2, 104.6 (2C), 103.8 (2C), 100.1, 60.9, 56.1 (2C), 55.3 (2C); Mass (+TOF): 331.538 [M+1], 353.536 [M+Na]; Anal. Calcd for C<sub>19</sub>H<sub>22</sub>O<sub>5</sub>: C, 69.09; H, 6.67%; Found: C, 69.07; H, 6.70%.

***trans*-1-(3, 4-Dimethylphenyl)-2-(3, 4, 5-trimethoxyphenyl)-ethene (23)**<sup>52</sup>

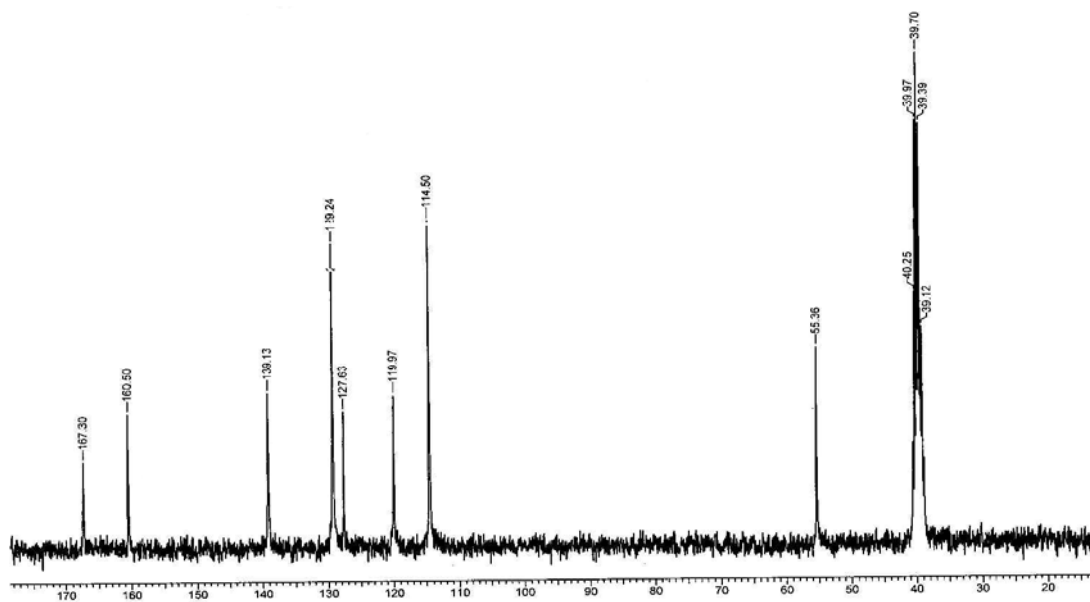
Off- white solid; <sup>1</sup>H NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 50 MHz): δ 7.29 (d, J=2 Hz, 1H), 7.24 (dd, J=8 Hz, 2Hz, 1H), 7.12 (d, J=8 Hz, 1H), 7.01 (d, J=16 Hz, 1H), 6.93 (d, J=16 Hz, 1H), 6.72 (s, 2H), 3.93 (s, 6H), 3.88 (s, 3H), 2.31 (s, 3H), 2.29 (s, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 100 MHz): 153.4 (2C), 137.9, 136.6, 136.1, 134.9, 133.4, 129.9, 128.2, 127.7, 127.5, 124.0, 103.6 (2C), 60.8, 56.1 (2C), 19.9, 19.6; IR (chloroform): 3020, 1653, 758 cm<sup>-1</sup>; Mass (+TOF): 299.890 [M+1], 321.825 [M+Na], 337.756 [M+K]; Anal. Calcd for C<sub>19</sub>H<sub>22</sub>O<sub>3</sub>: C, 76.48; H, 7.43 %; Found: C, 76.46; H, 7.41%.

## Appendix-5.A

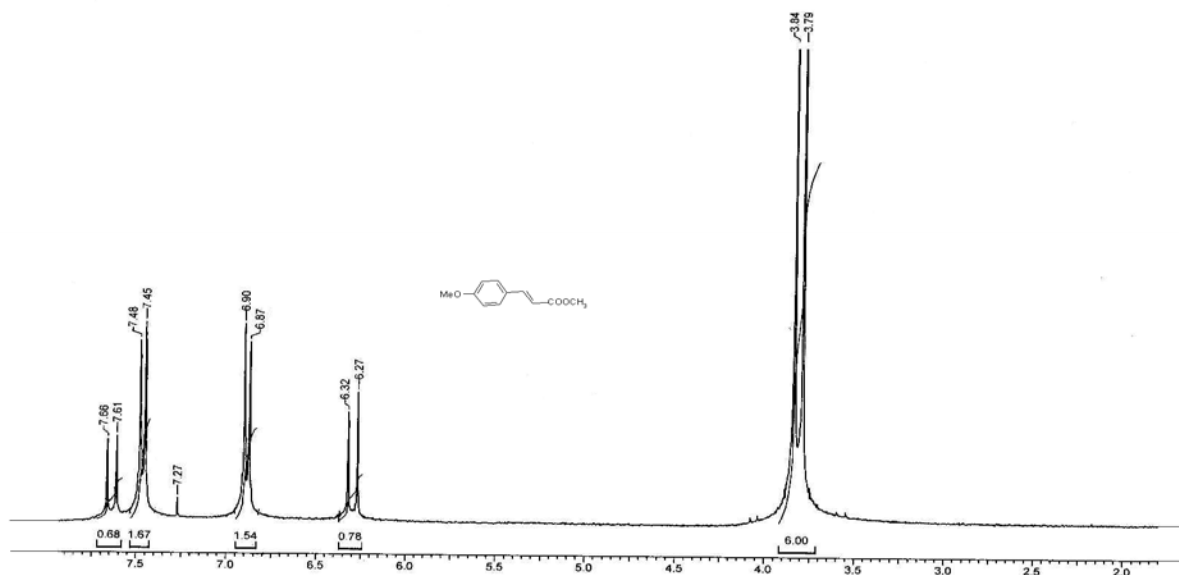
### $^1\text{H}$ NMR Spectrum of the Compound 1 ( $\text{CDCl}_3 + \text{CCl}_4$ , 75 MHz)



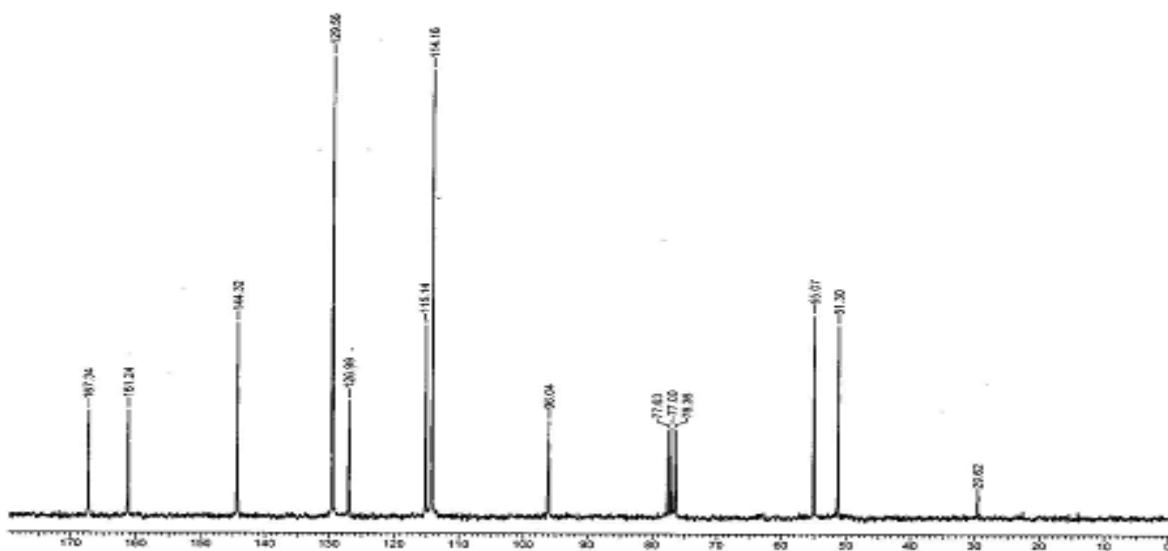
### $^{13}\text{C}$ NMR Spectrum of the Compound 1 ( $\text{CDCl}_3 + \text{CCl}_4$ , 75 MHz)



**<sup>1</sup>H NMR Spectrum of the Compound 2 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**

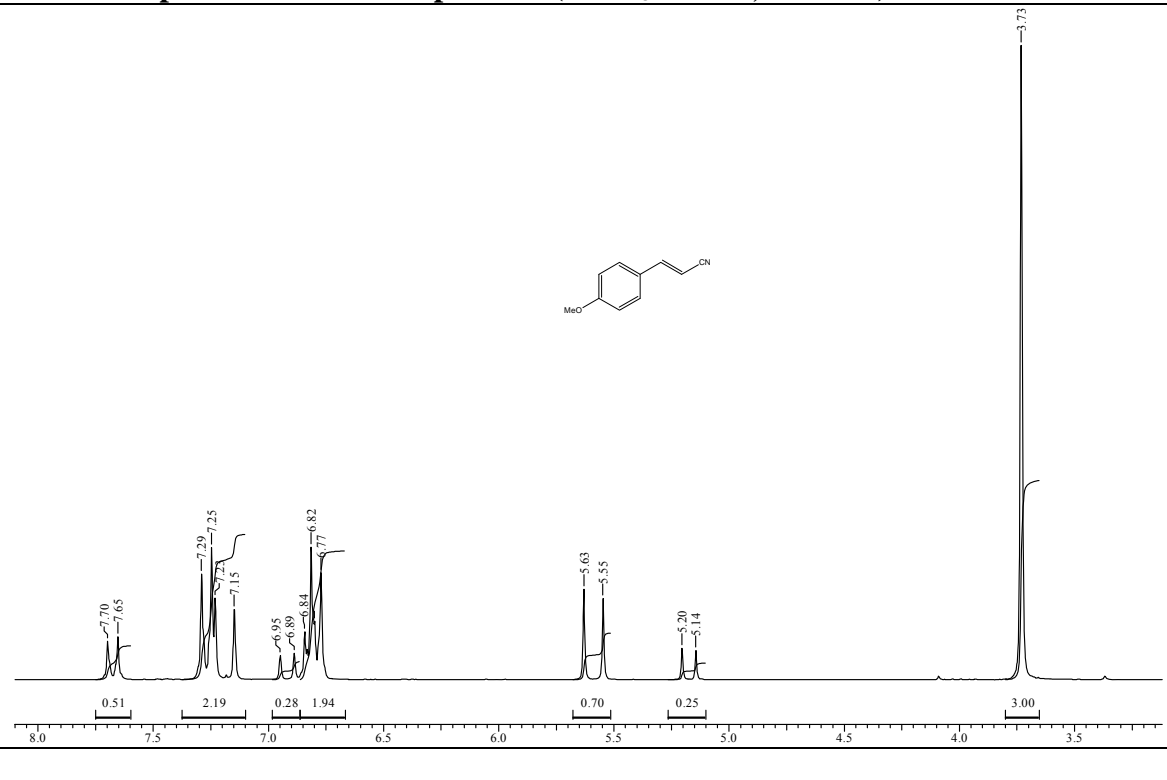


**<sup>13</sup>C NMR Spectrum of the Compound 2 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**

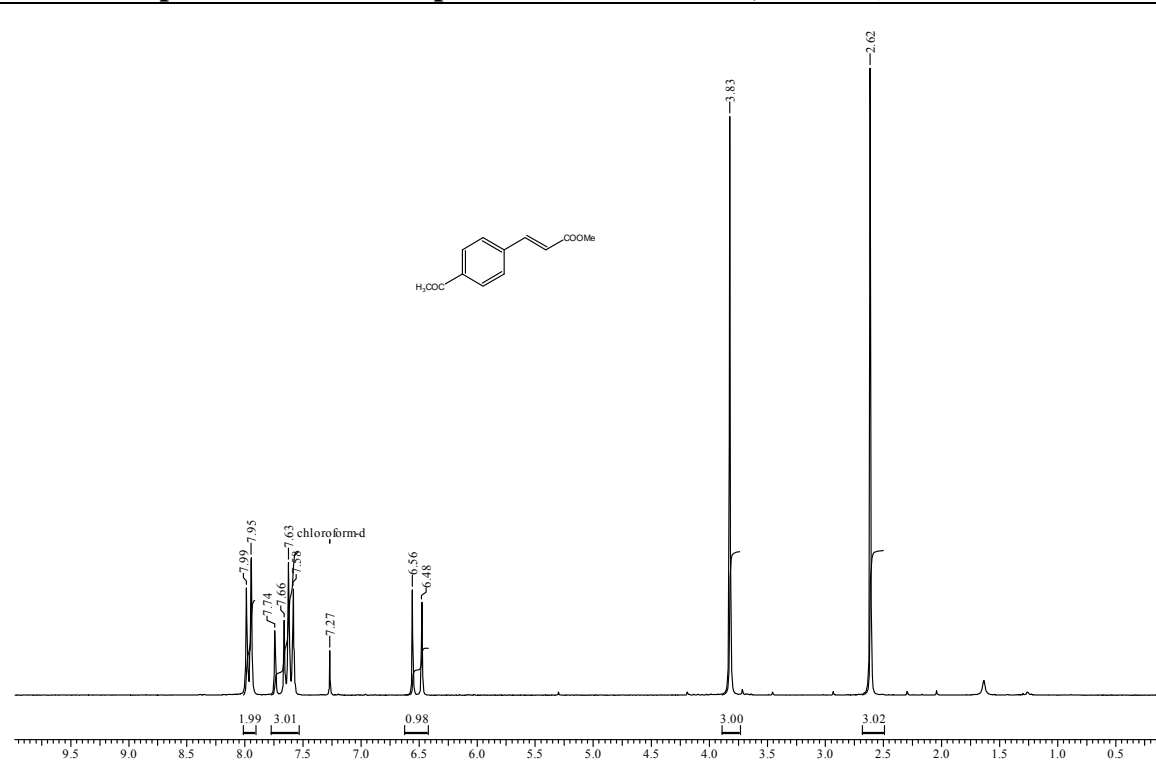




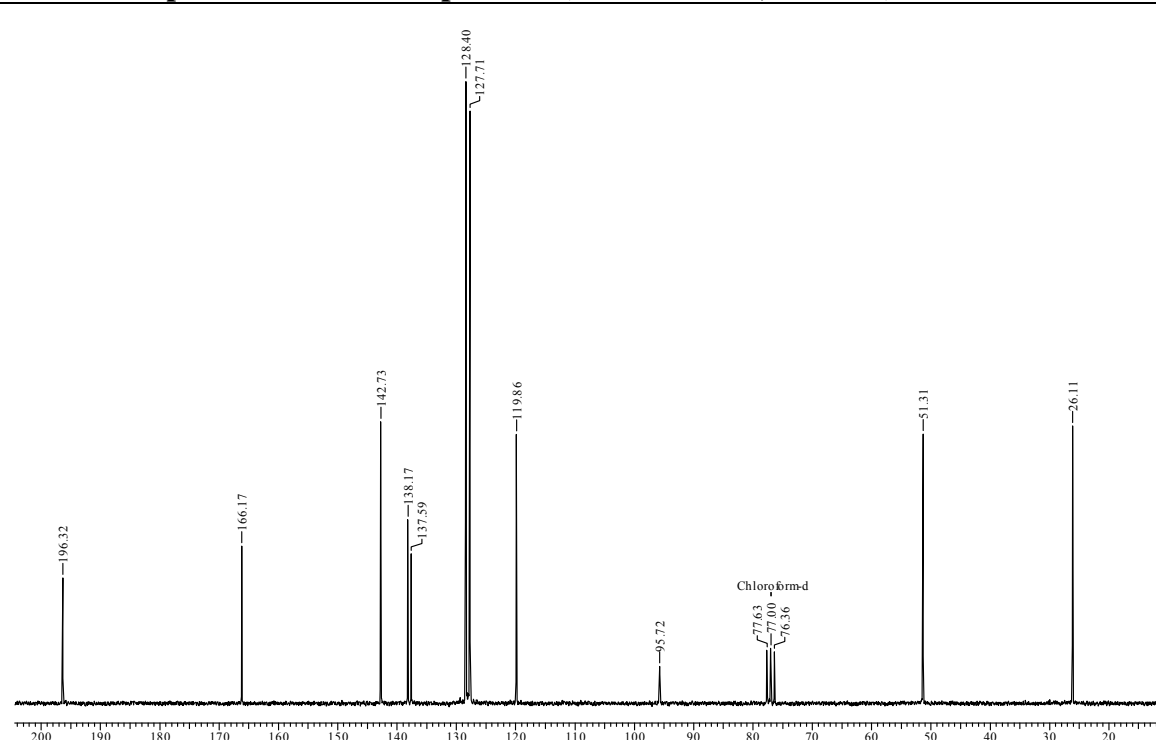
**<sup>1</sup>H NMR Spectrum of the Compound 3 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



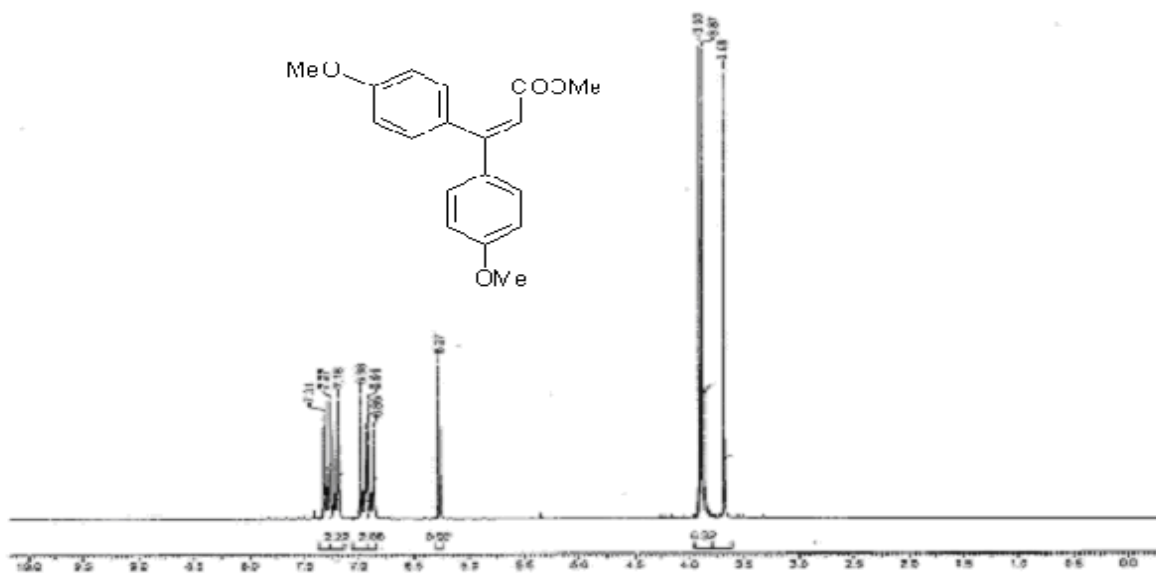
**<sup>1</sup>H NMR Spectrum of the Compound 4 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



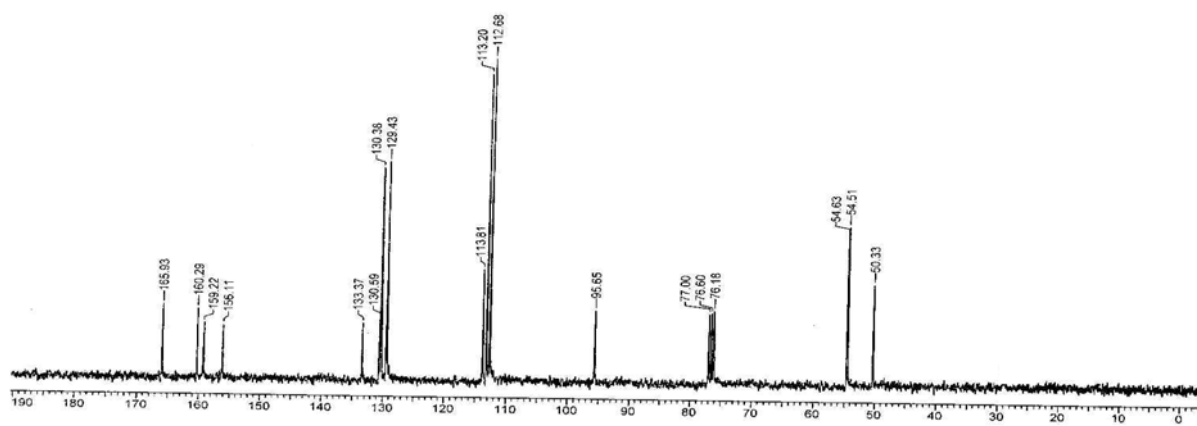
**<sup>13</sup>C NMR Spectrum of the Compound 4 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



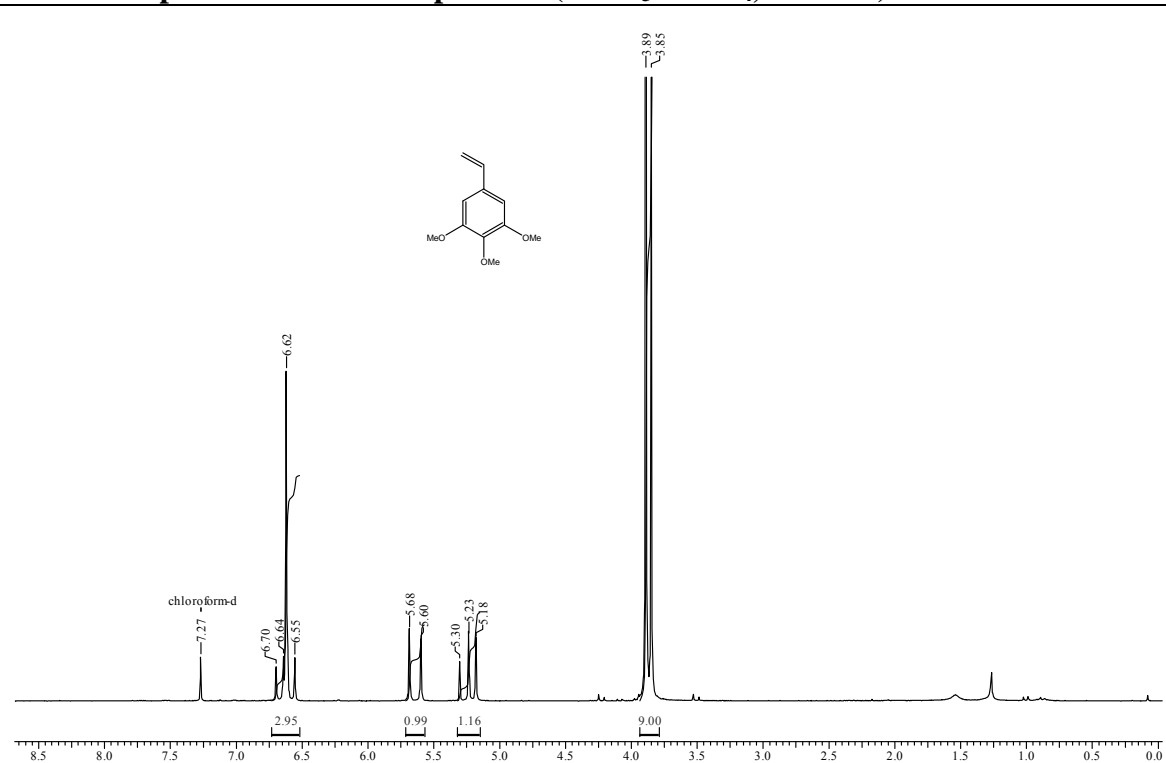
**<sup>1</sup>H NMR Spectrum of the Compound 5 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



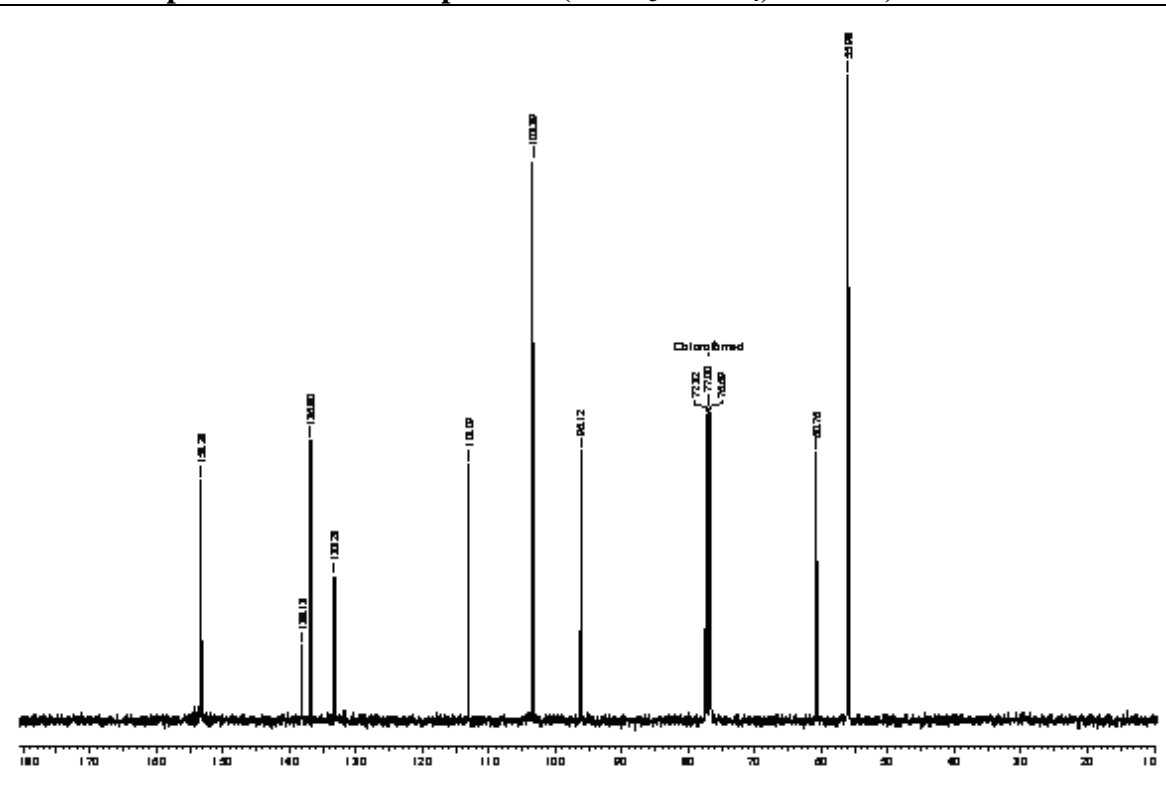
**<sup>13</sup>C NMR Spectrum of the Compound 5 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 75 MHz)**



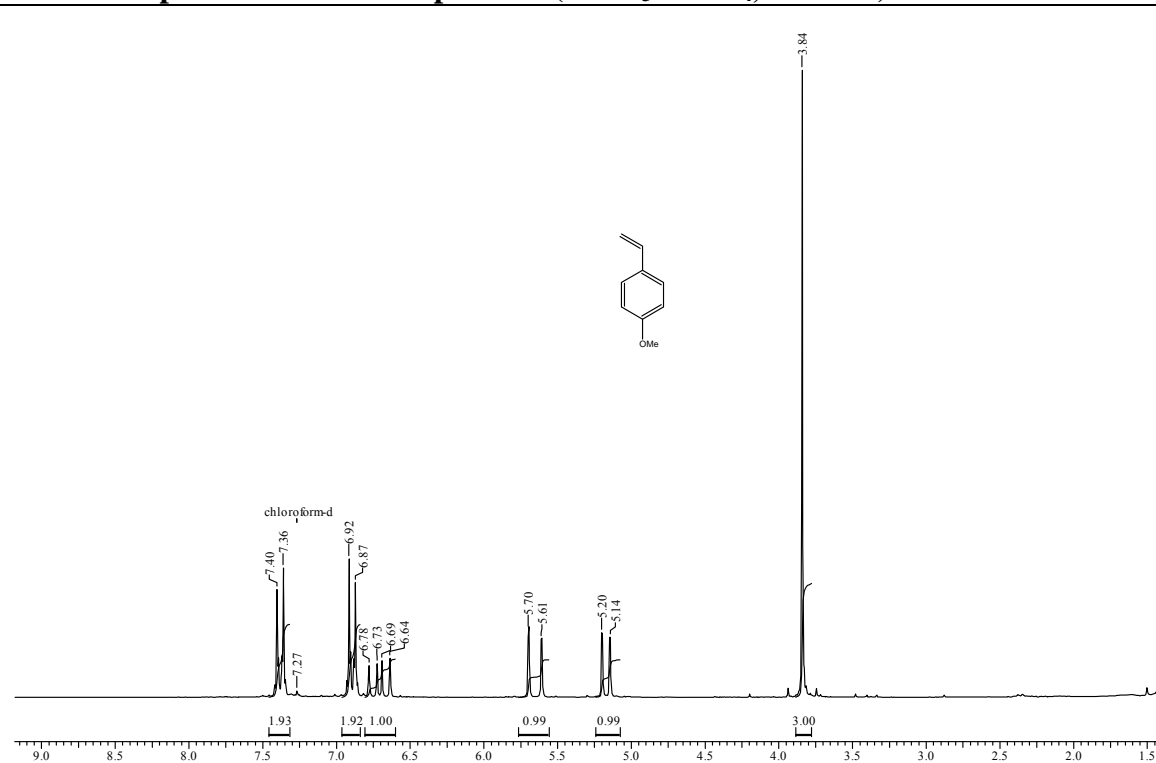
**<sup>1</sup>H NMR Spectrum of the Compound 6 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



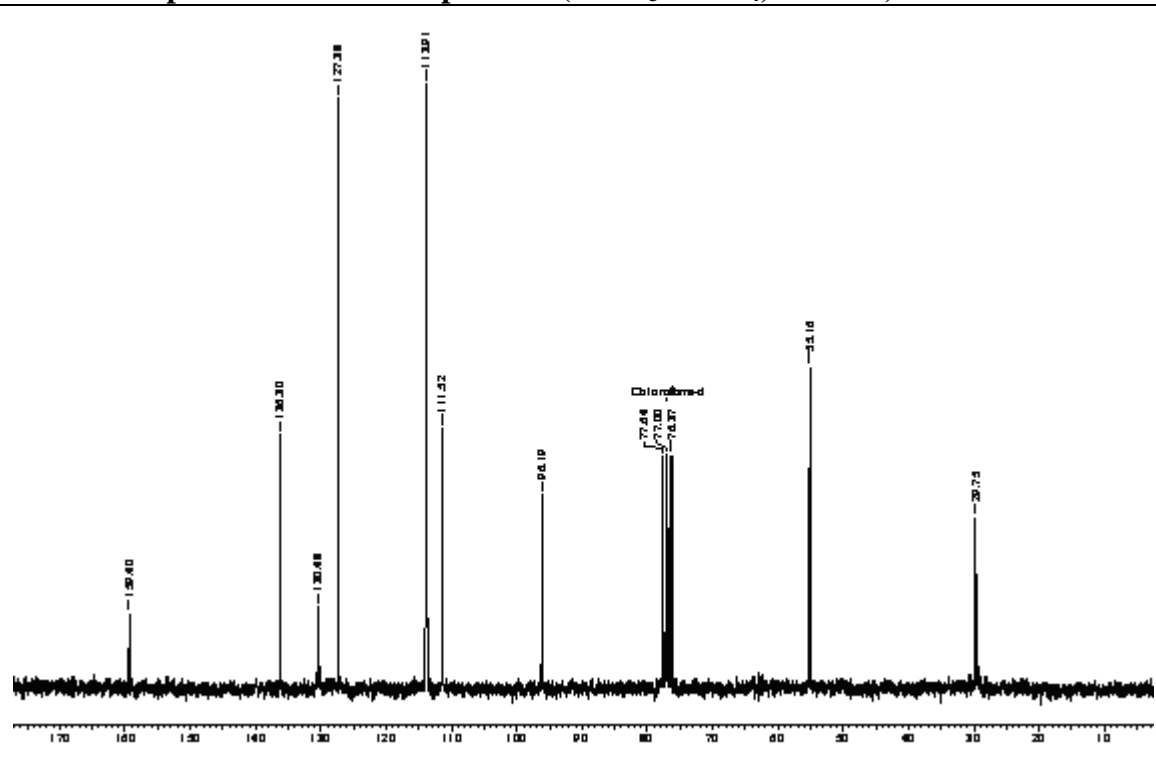
**<sup>13</sup>C NMR Spectrum of the Compound 6 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



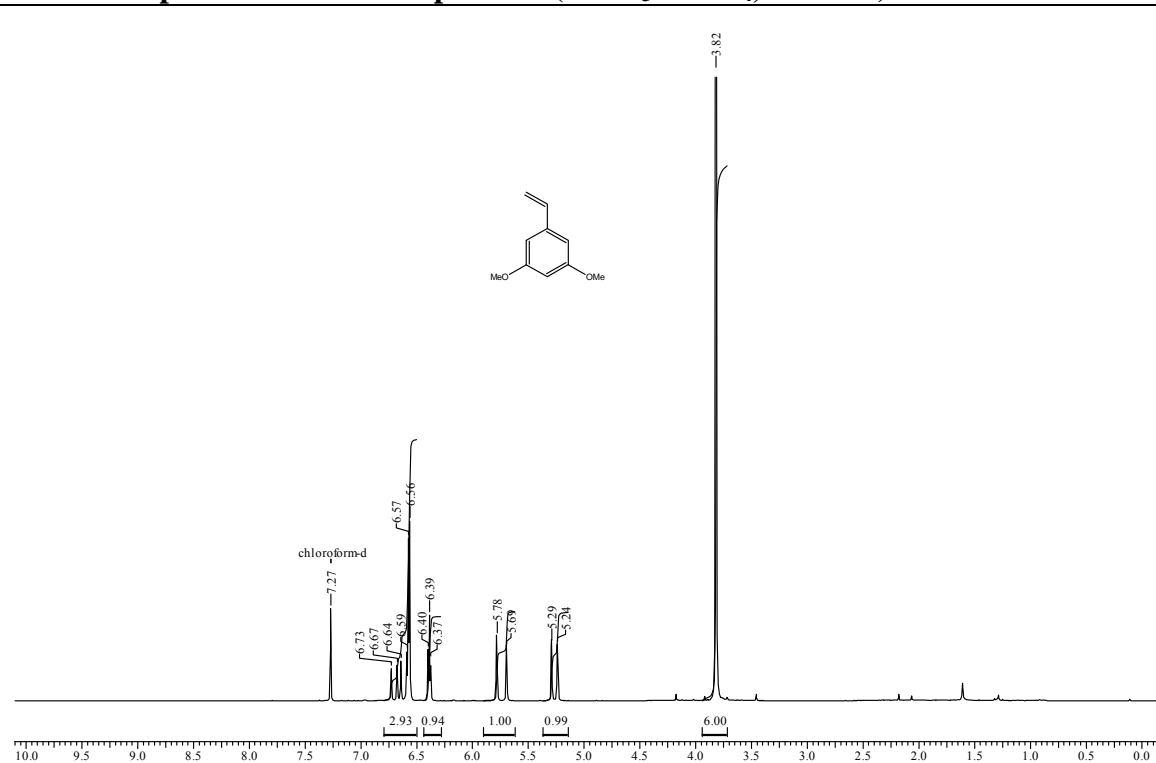
**<sup>1</sup>H NMR Spectrum of the Compound 7 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



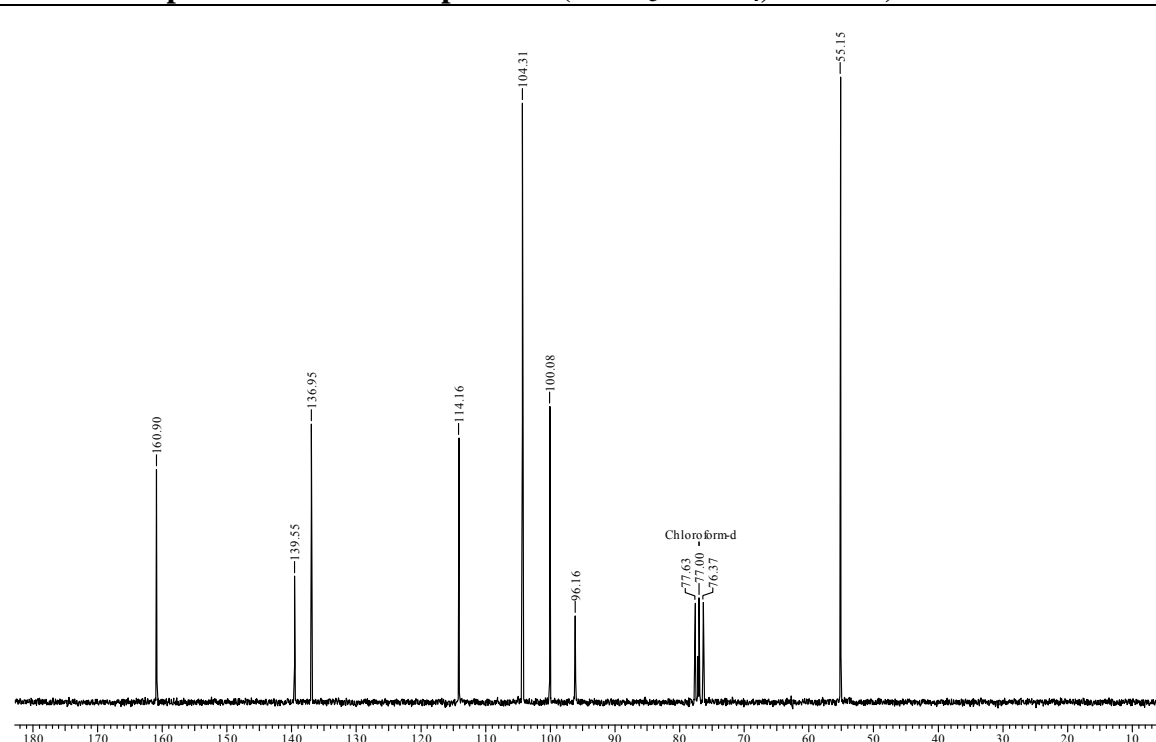
**<sup>13</sup>C NMR Spectrum of the Compound 7 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



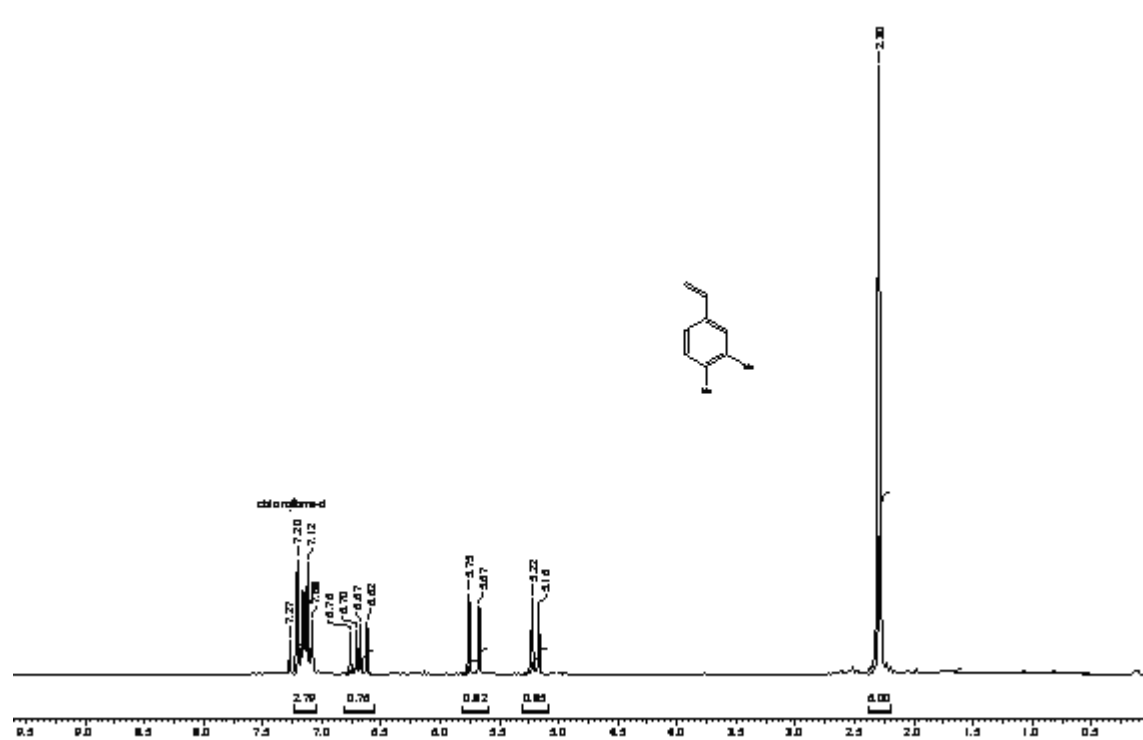
**<sup>1</sup>H NMR Spectrum of the Compound 8 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



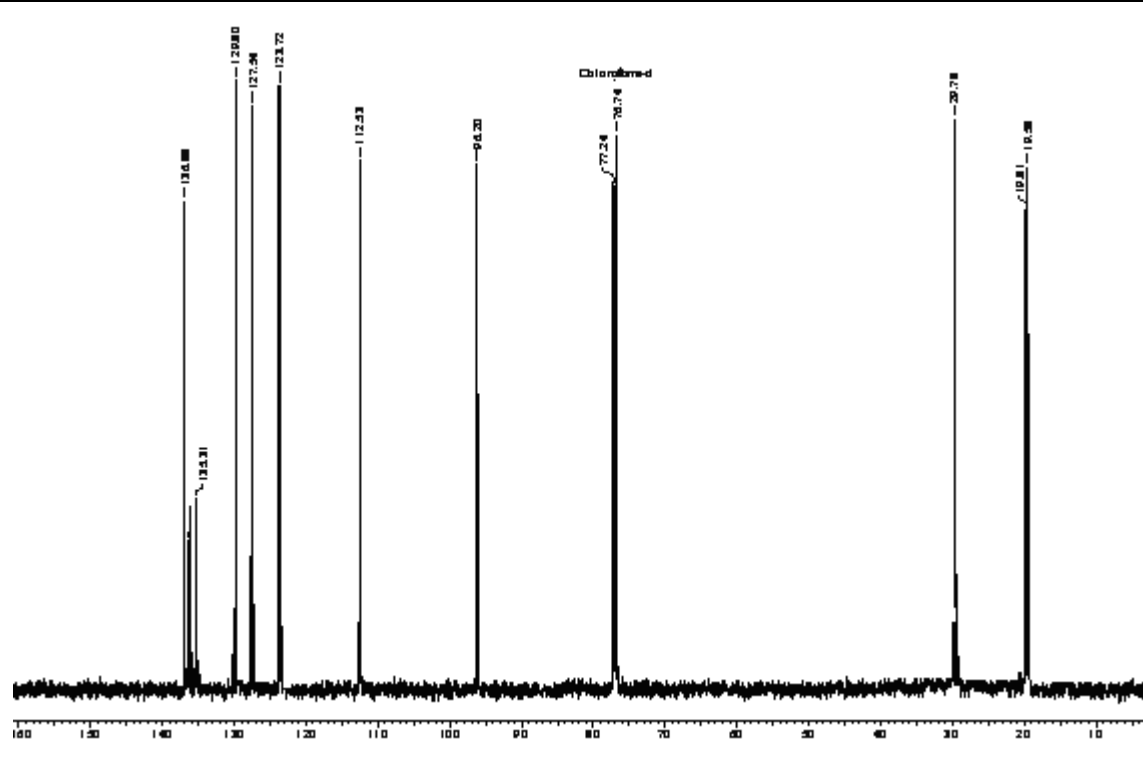
**<sup>13</sup>C NMR Spectrum of the Compound 8 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



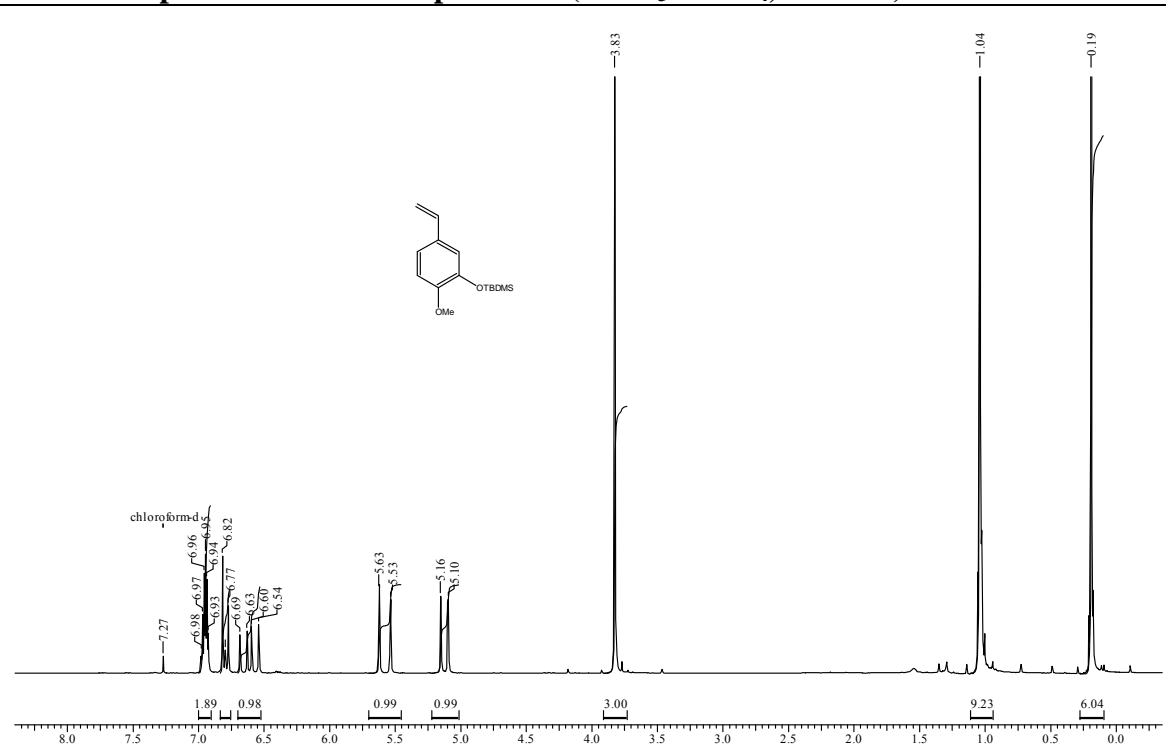
**<sup>1</sup>H NMR Spectrum of the Compound 9 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



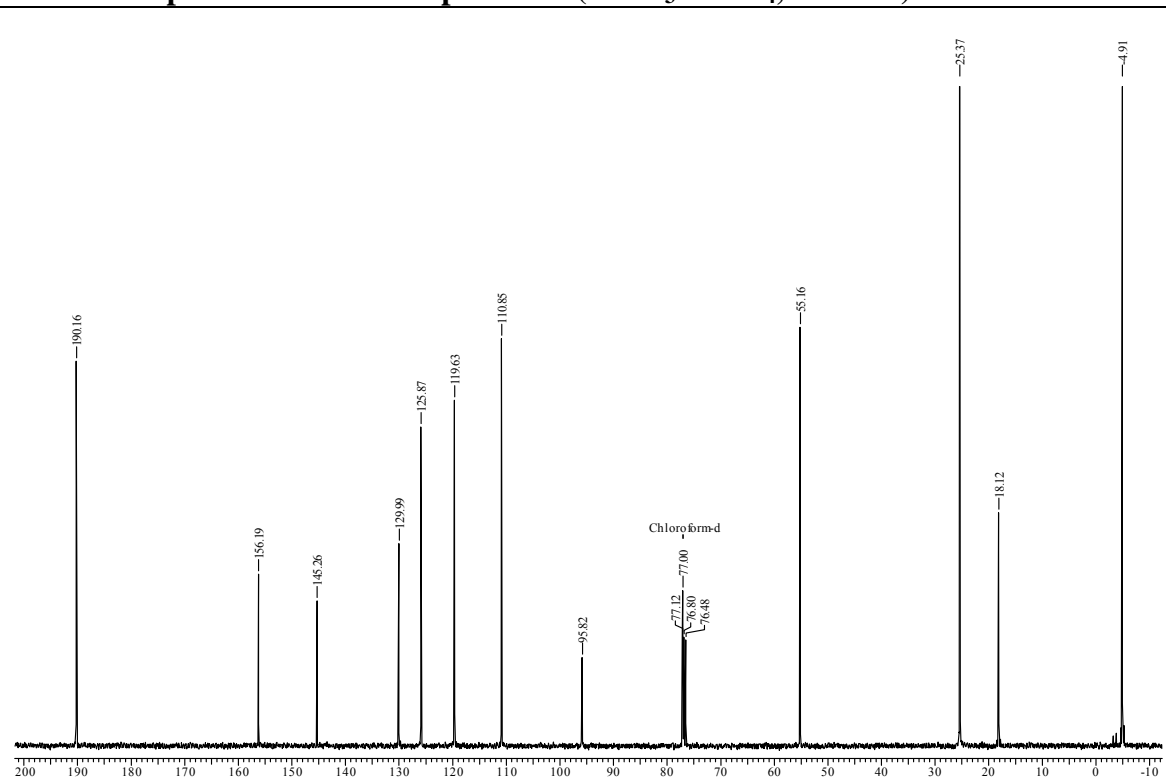
**<sup>13</sup>C NMR Spectrum of the Compound 9 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



**<sup>1</sup>H NMR Spectrum of the Compound 11 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**

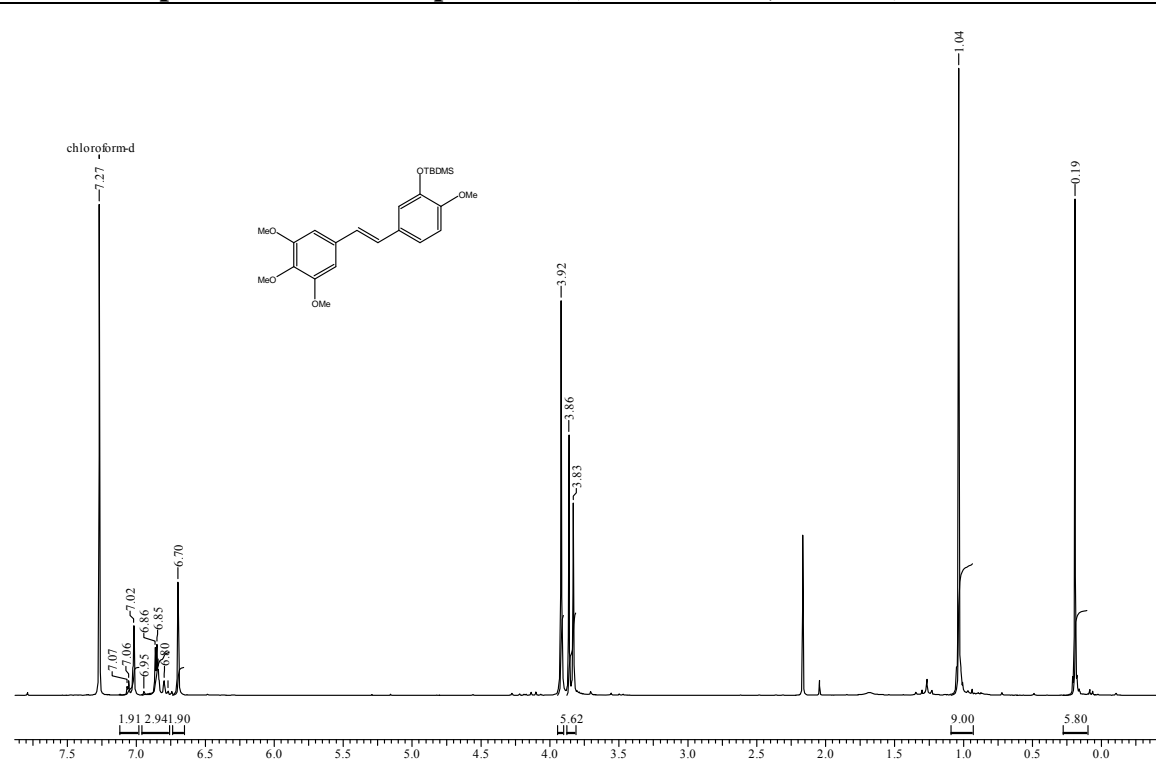


**<sup>13</sup>C NMR Spectrum of the Compound 11 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**

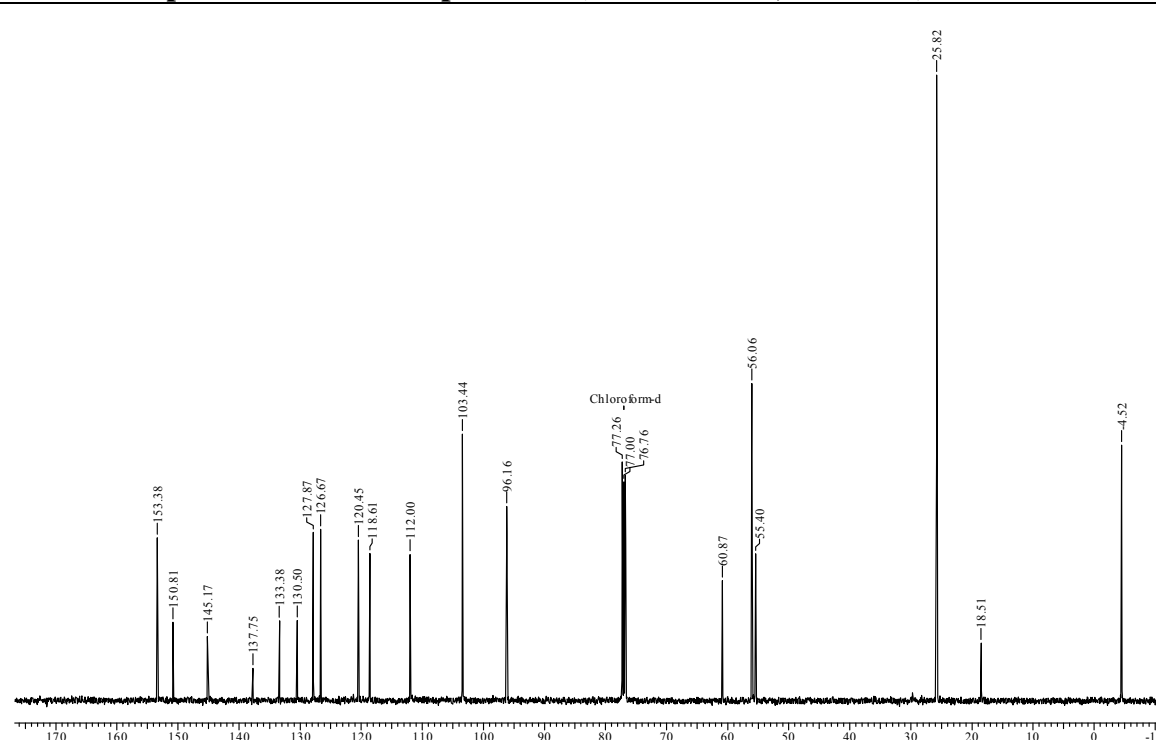




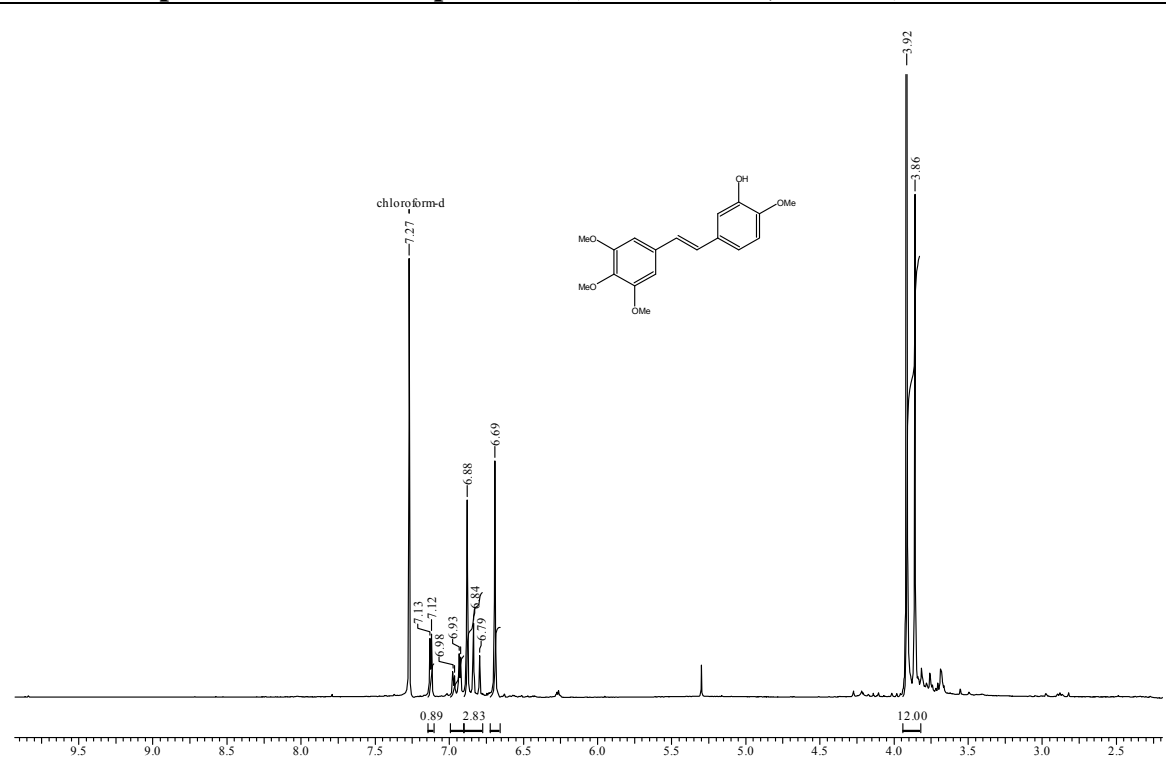
**<sup>1</sup>H NMR Spectrum of the Compound 12 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



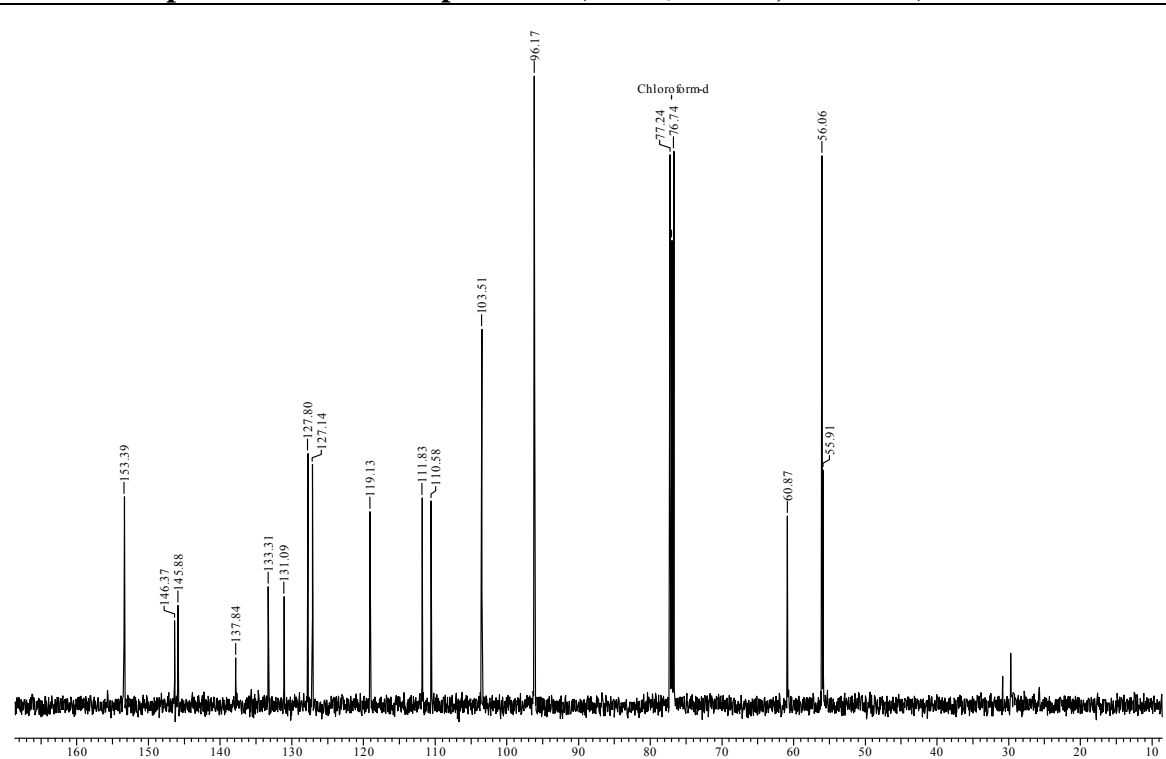
**<sup>13</sup>C NMR Spectrum of the Compound 12 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 100 MHz)**



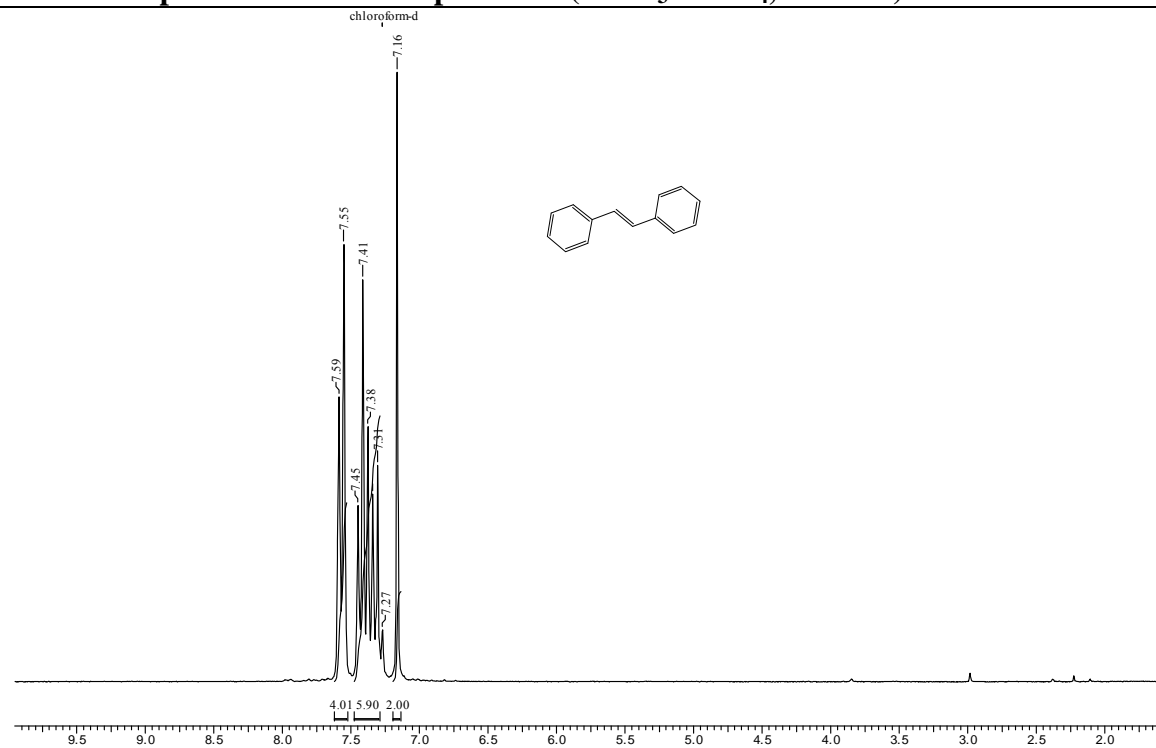
**<sup>1</sup>H NMR Spectrum of the Compound 13 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



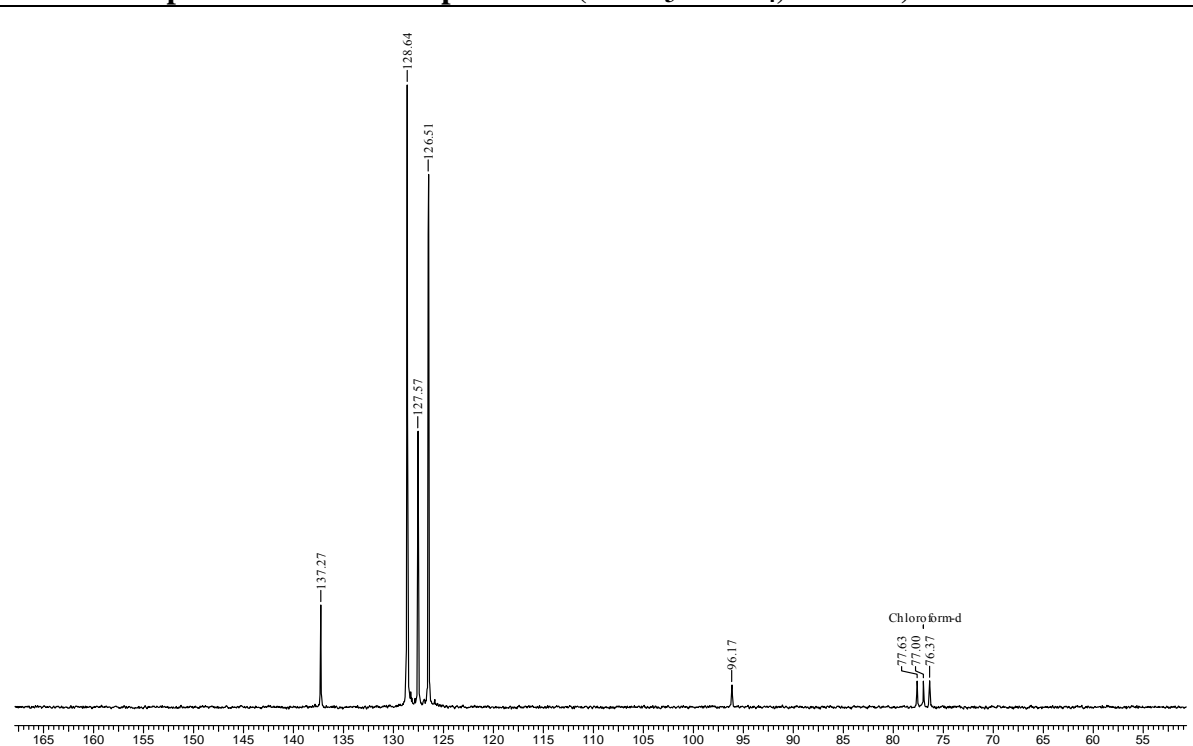
**<sup>13</sup>C NMR Spectrum of the Compound 13 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 100 MHz)**



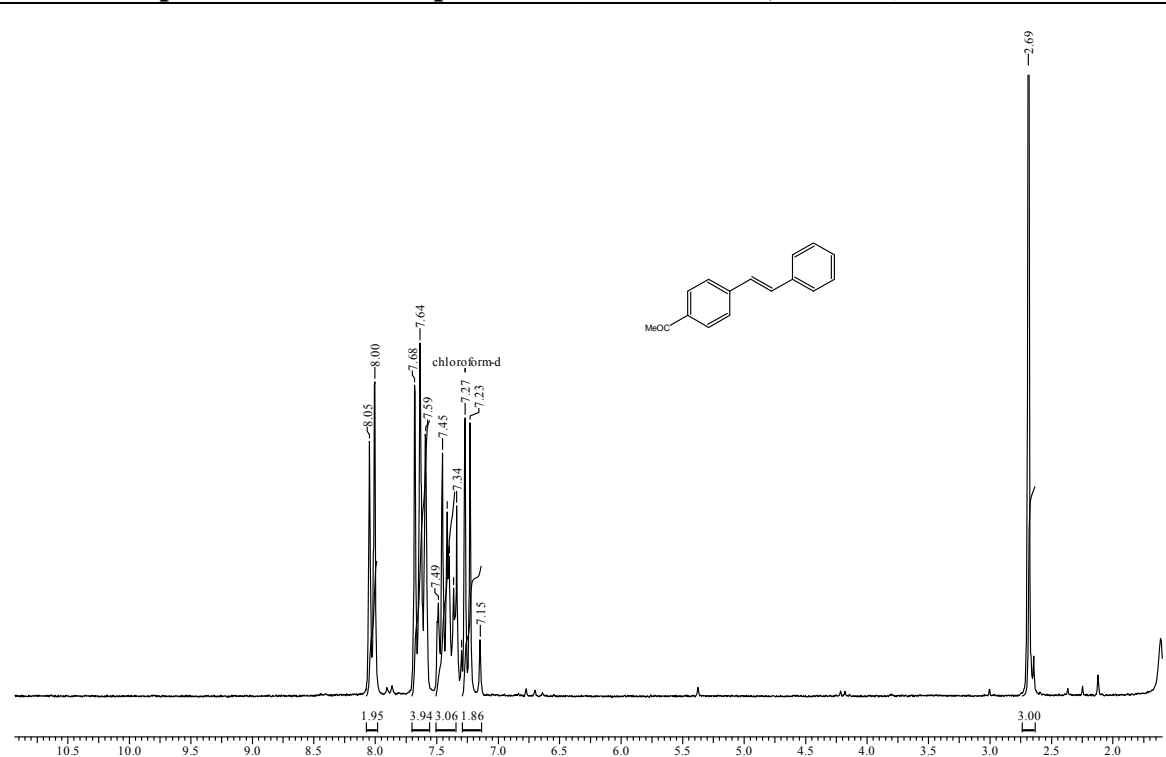
**<sup>1</sup>H NMR Spectrum of the Compound 14 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



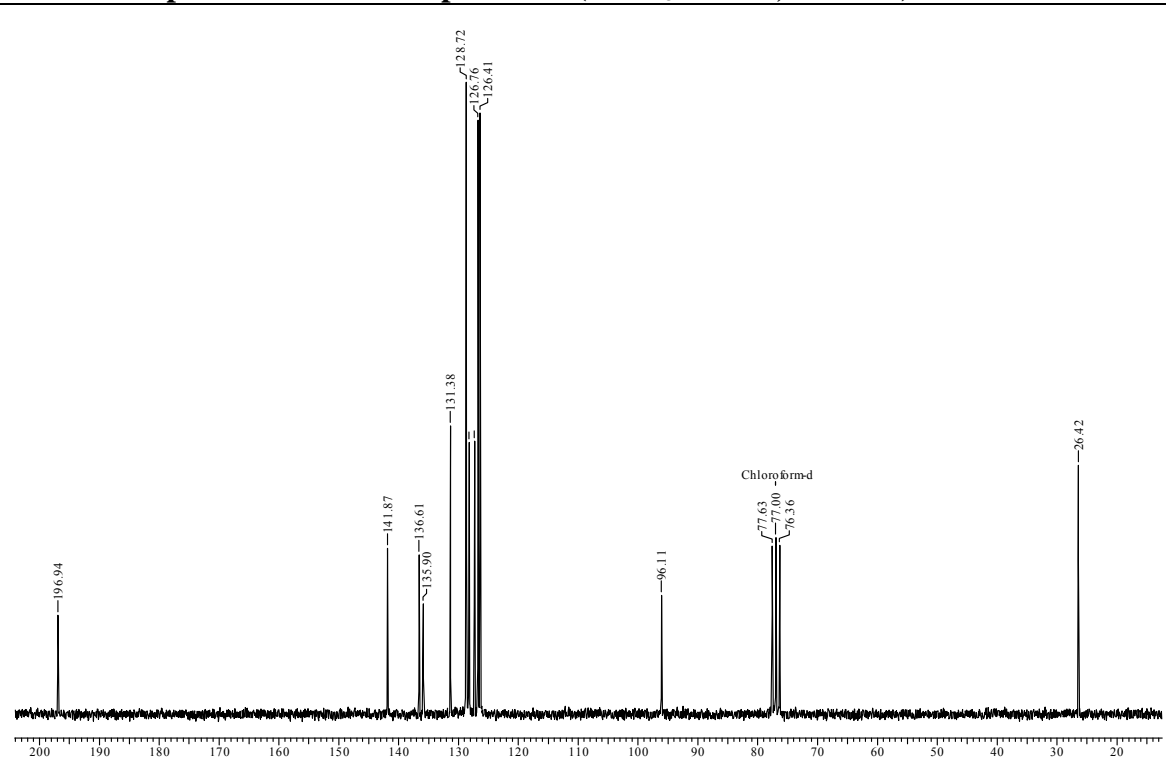
**<sup>13</sup>C NMR Spectrum of the Compound 14 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



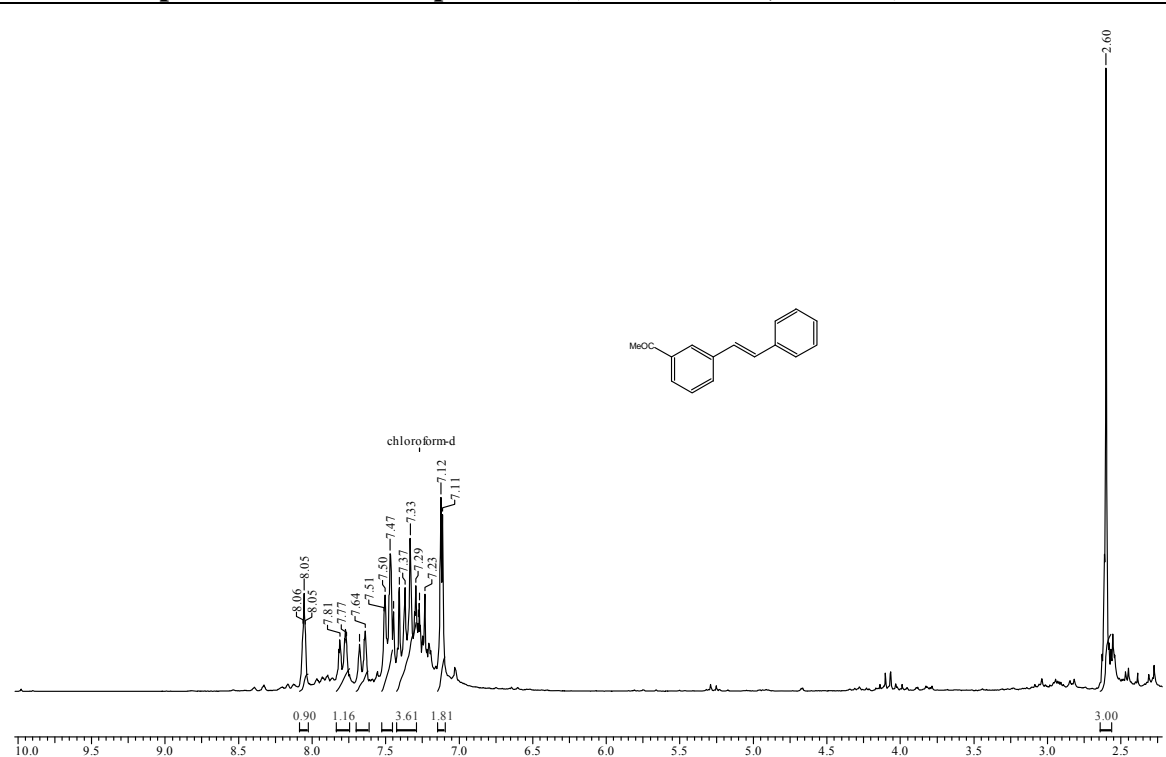
**<sup>1</sup>H NMR Spectrum of the Compound 15 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



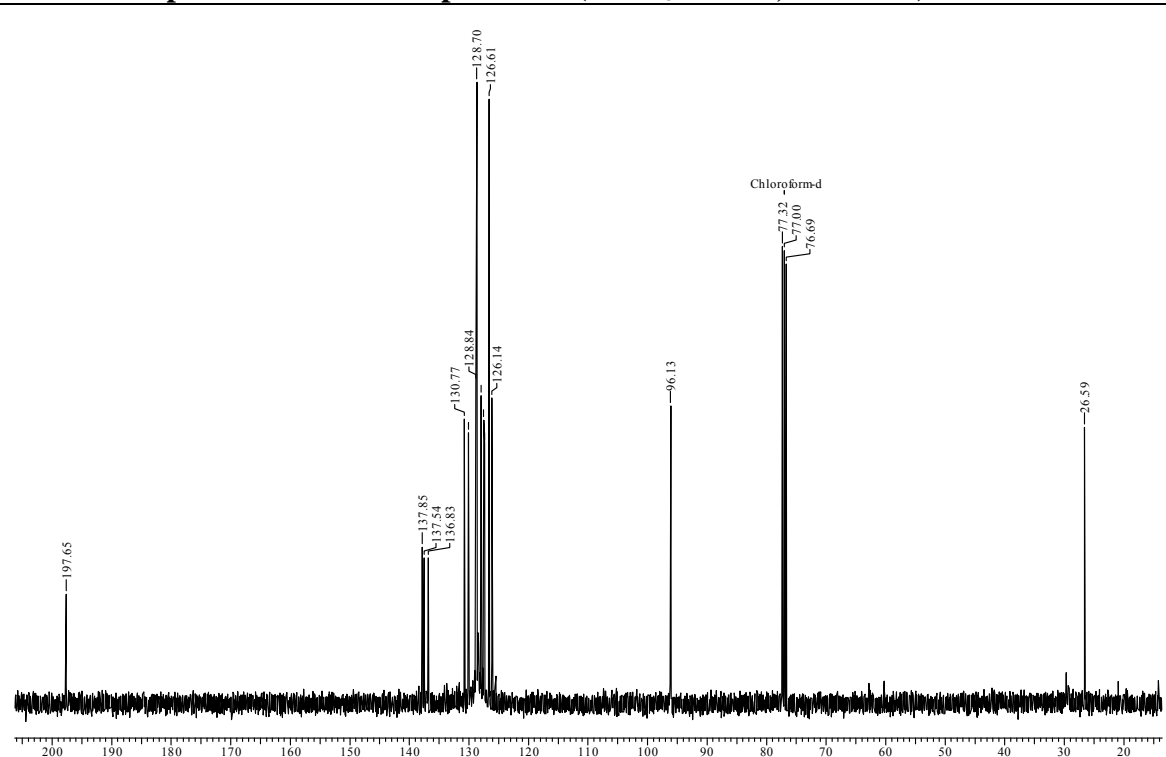
**<sup>13</sup>C NMR Spectrum of the Compound 15 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



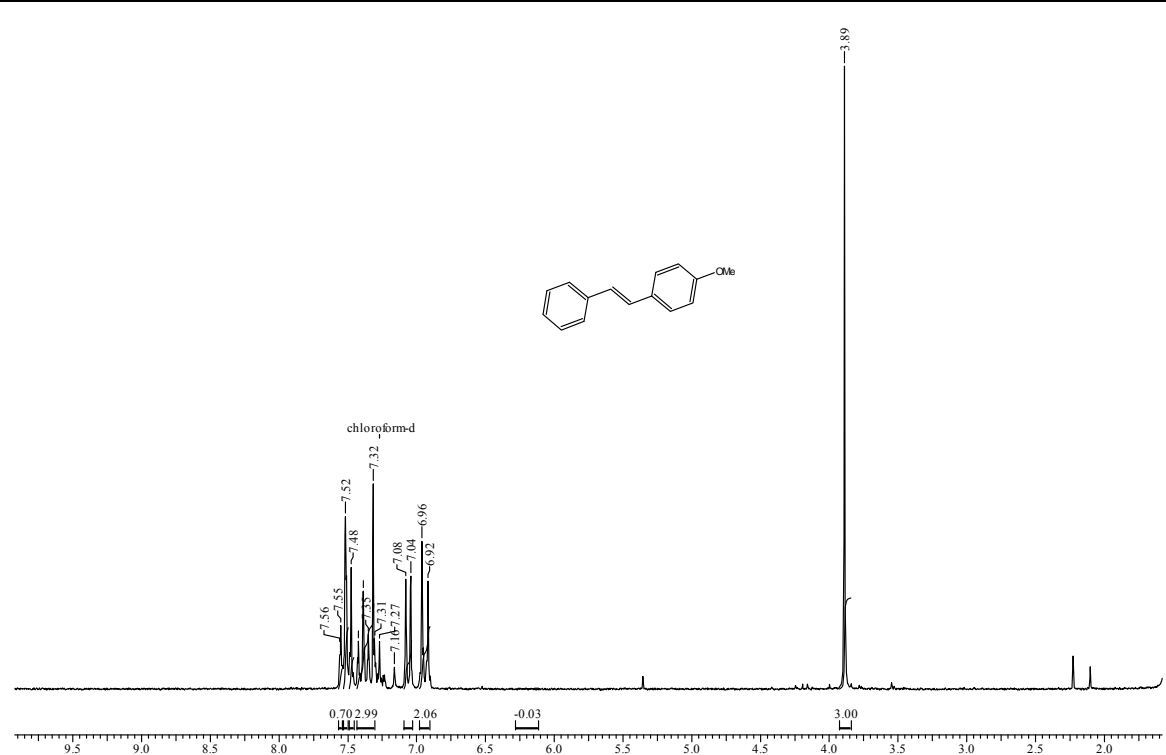
**<sup>1</sup>H NMR Spectrum of the Compound 16 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



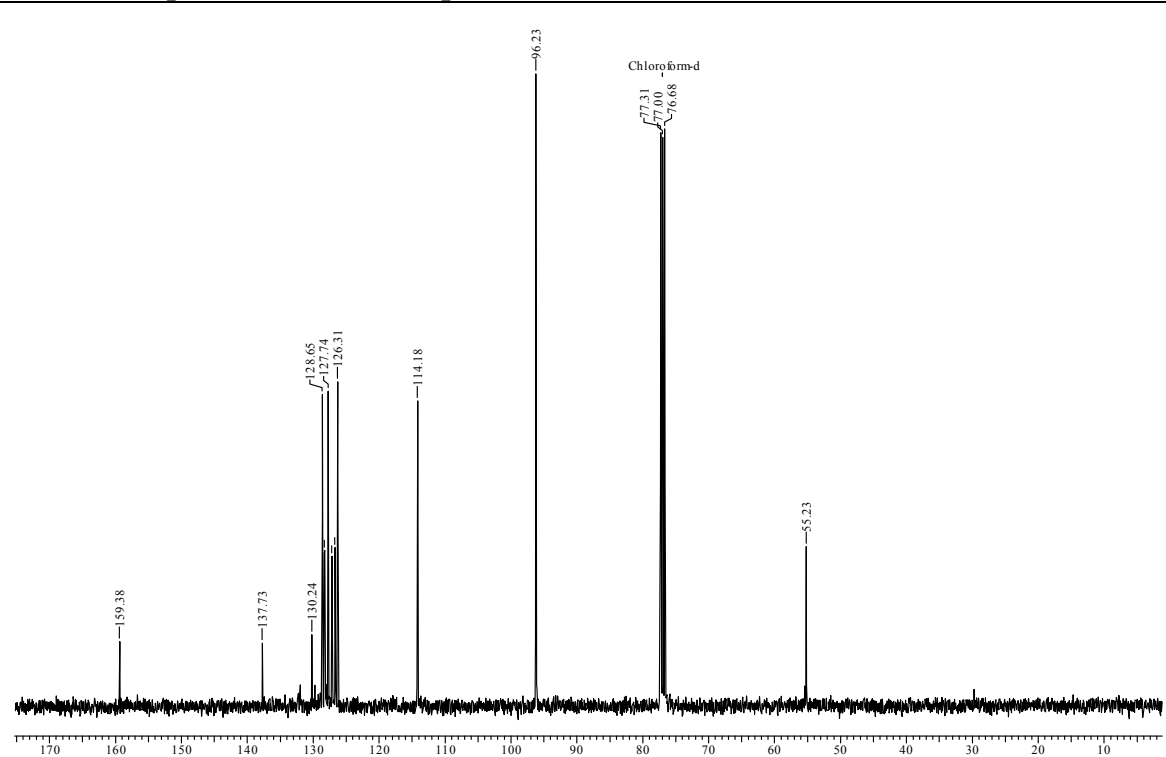
**<sup>13</sup>C NMR Spectrum of the Compound 16 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 100 MHz)**



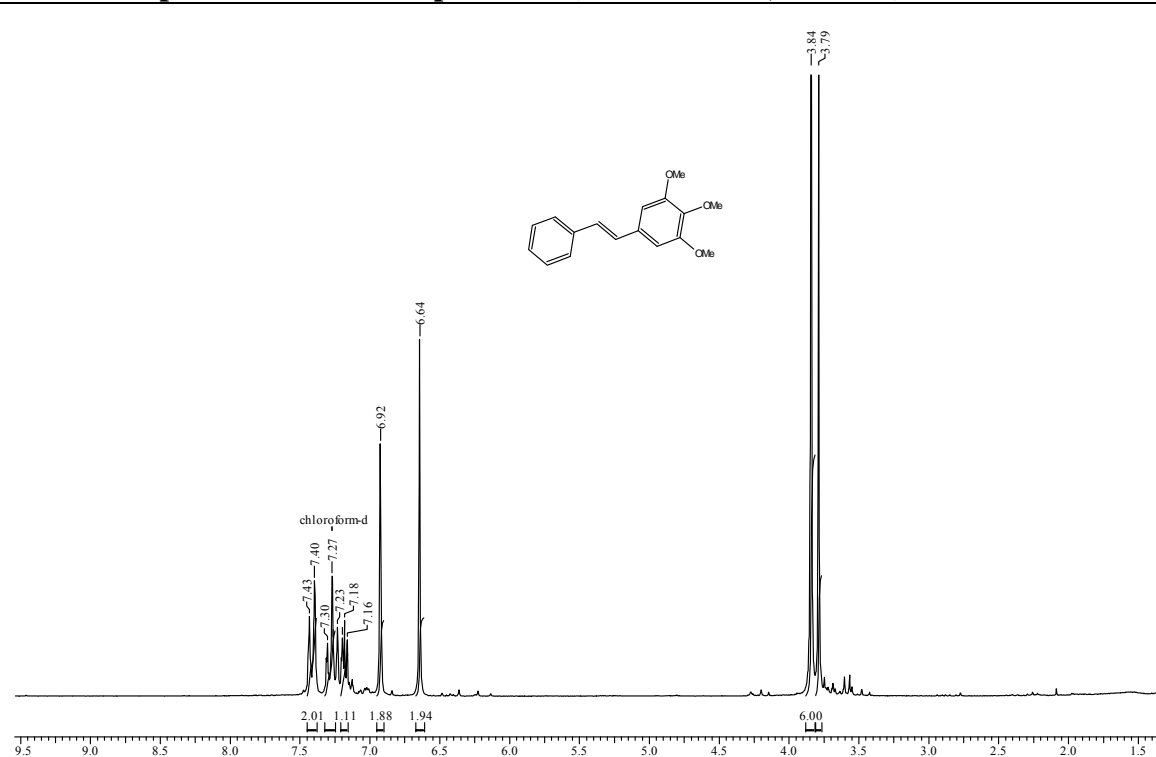
**<sup>1</sup>H NMR Spectrum of the Compound 17 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



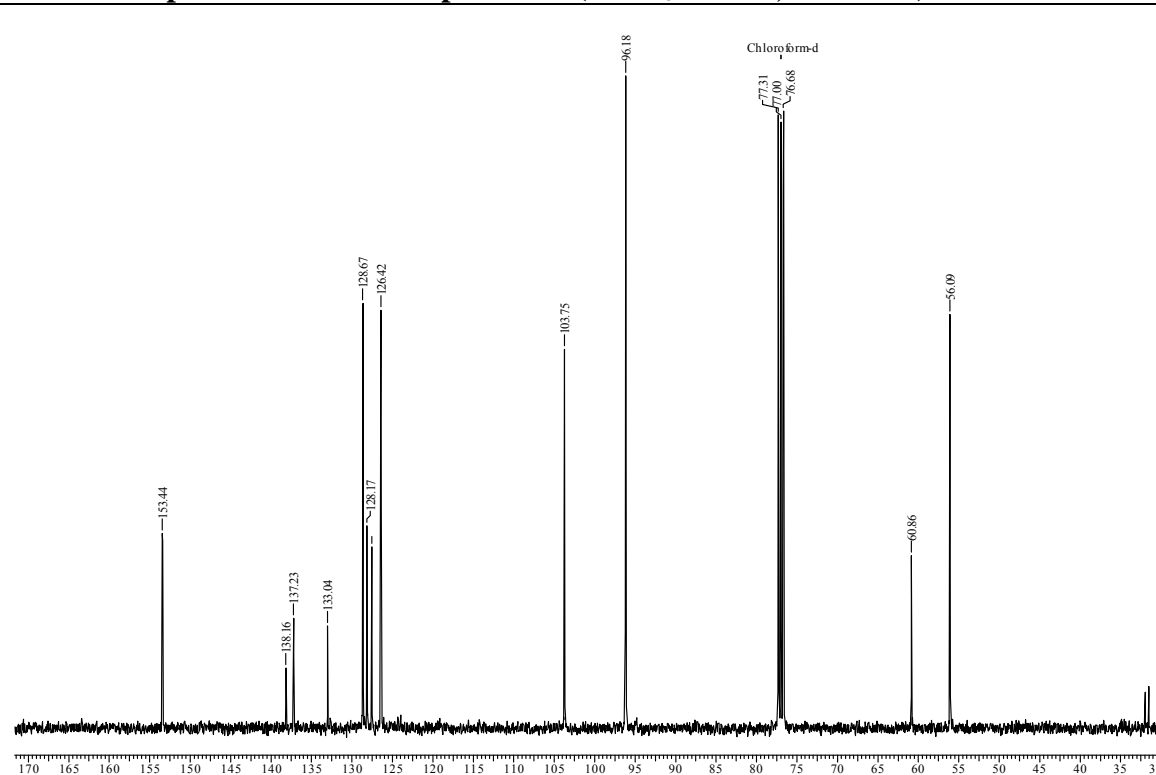
**<sup>13</sup>C NMR Spectrum of the Compound 17 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 100 MHz)**



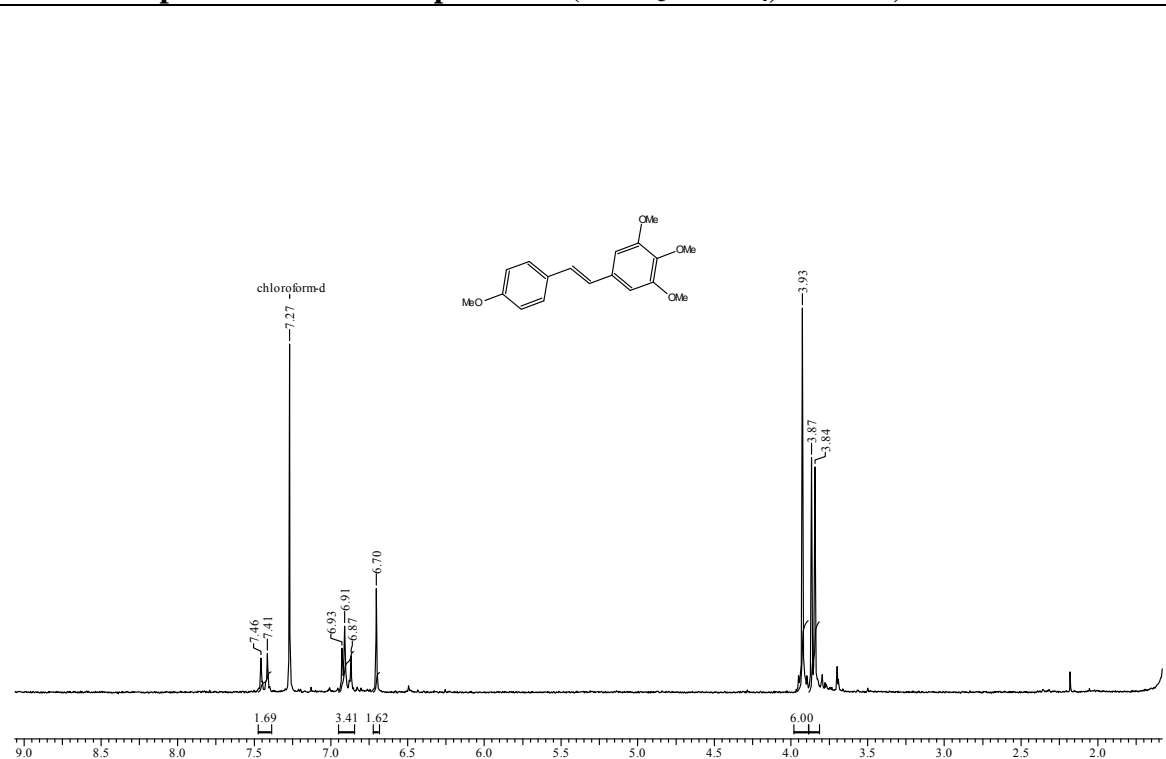
**<sup>1</sup>H NMR Spectrum of the Compound 18 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



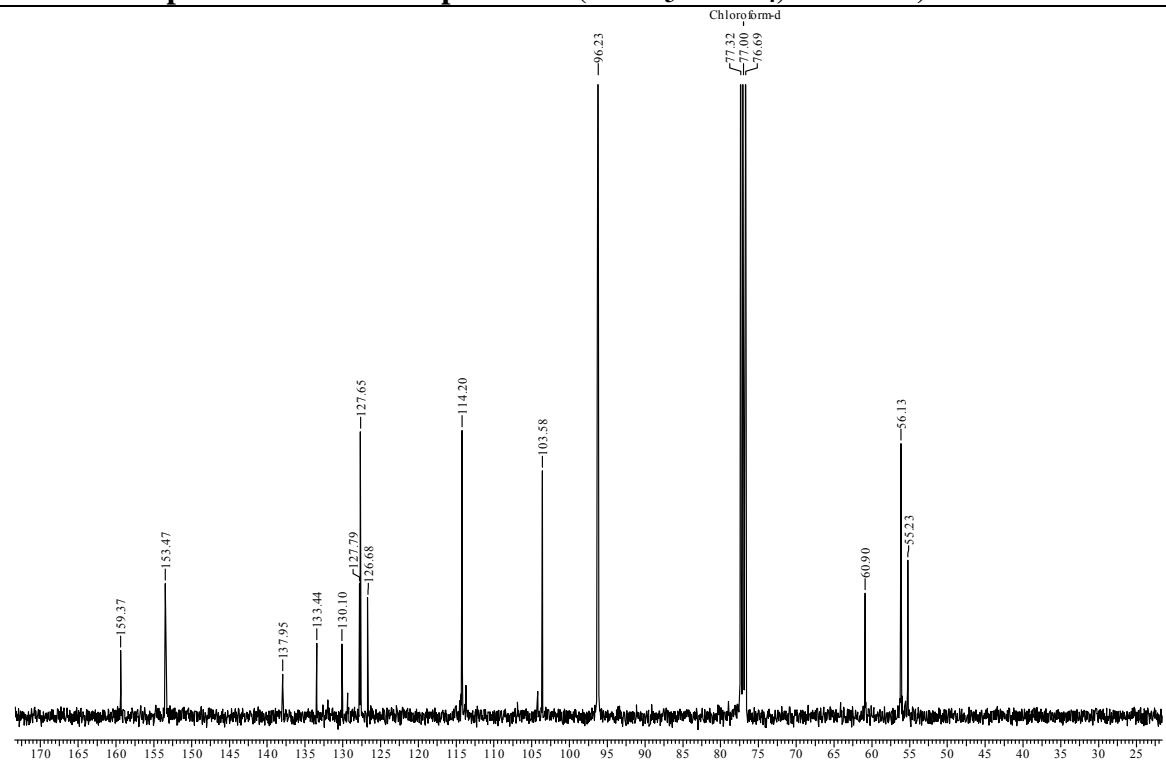
**<sup>13</sup>C NMR Spectrum of the Compound 18 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 100 MHz)**



**<sup>1</sup>H NMR Spectrum of the Compound 19 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**

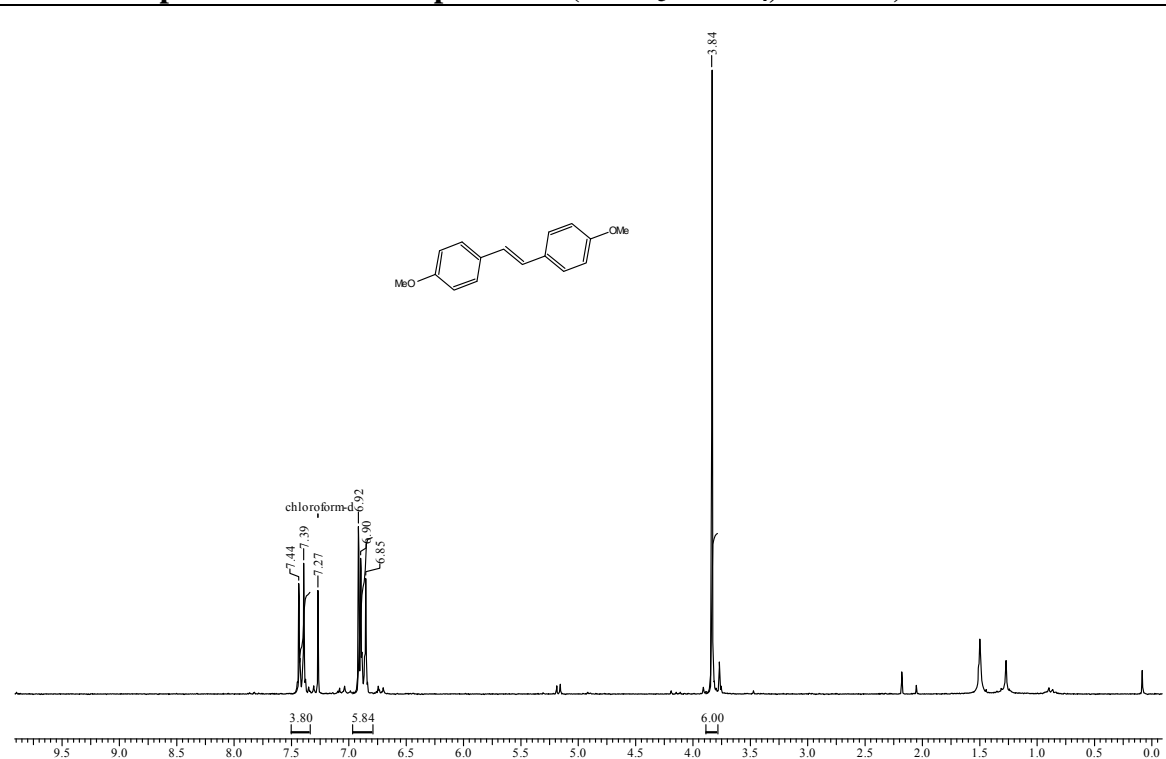


**<sup>13</sup>C NMR Spectrum of the Compound 19 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 100 MHz)**

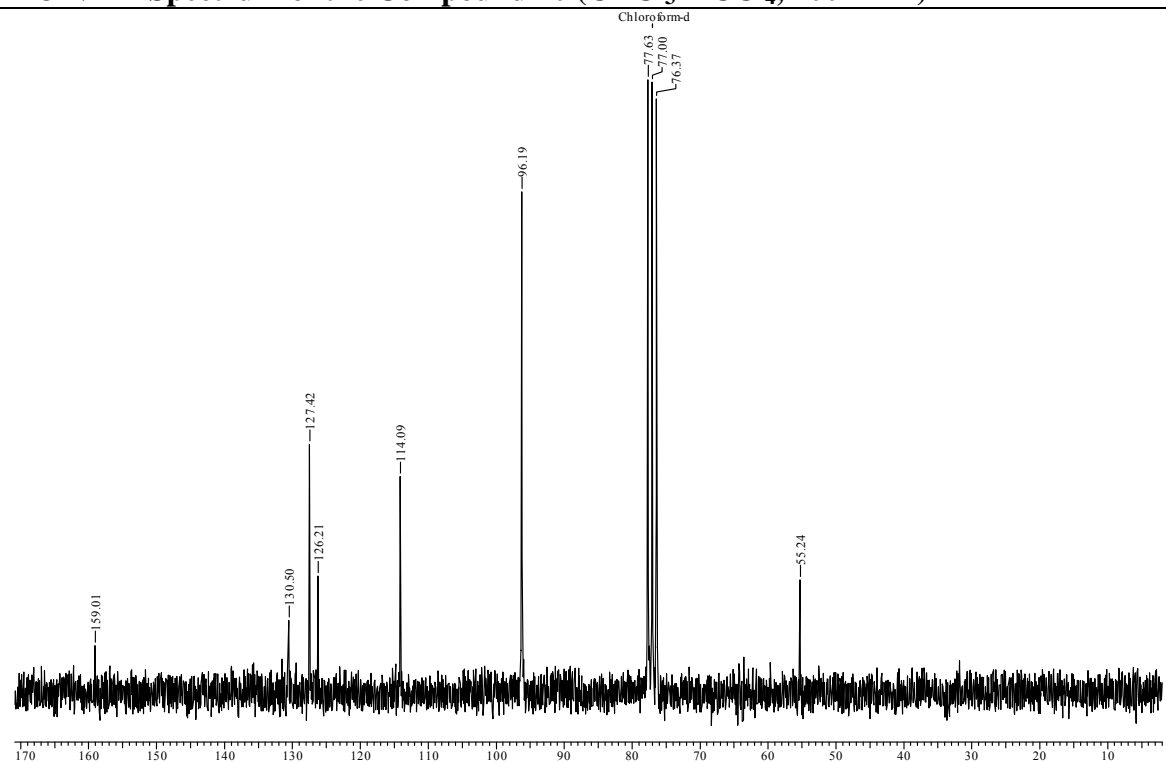




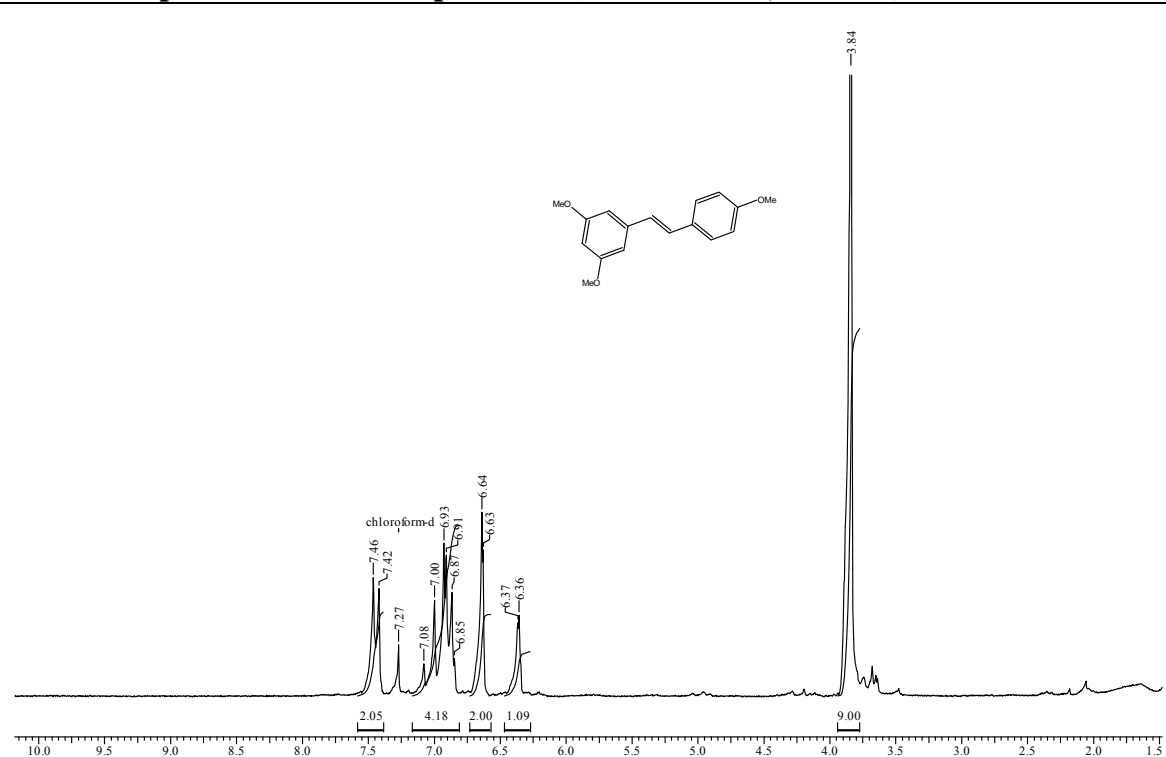
**<sup>1</sup>H NMR Spectrum of the Compound 20 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



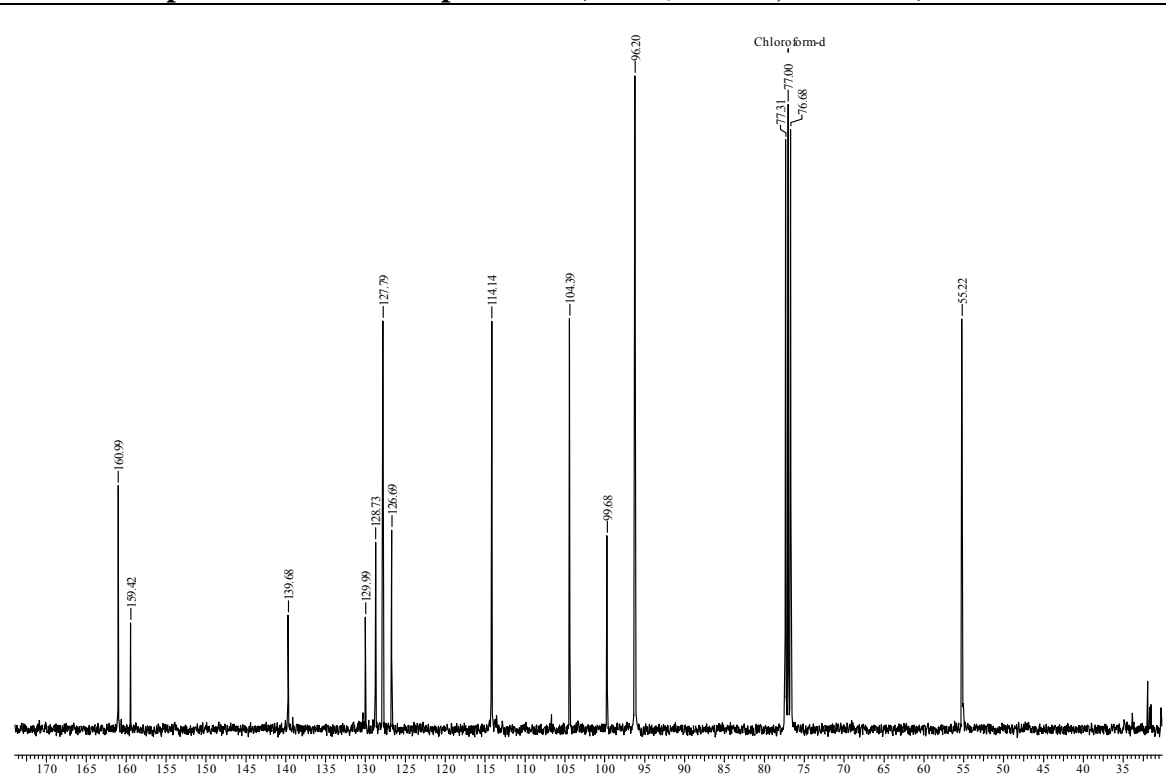
**<sup>13</sup>C NMR Spectrum of the Compound 20 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 100 MHz)**



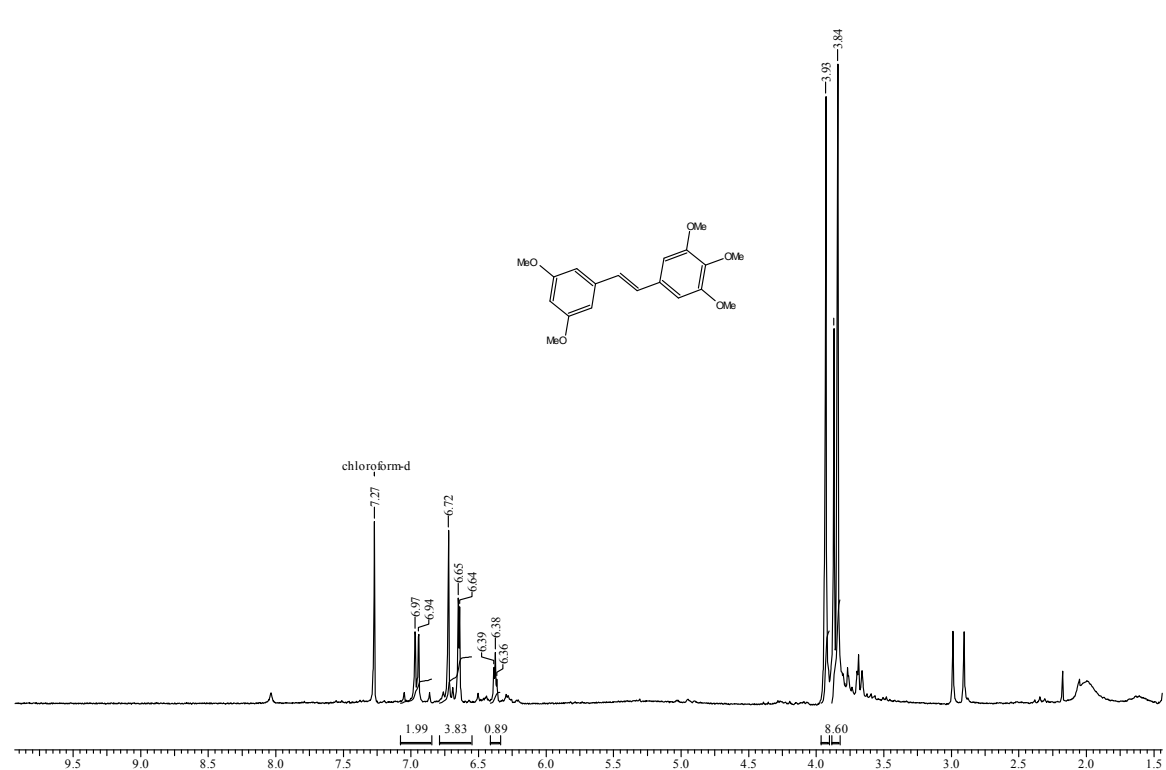
**<sup>1</sup>H NMR Spectrum of the Compound 21 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



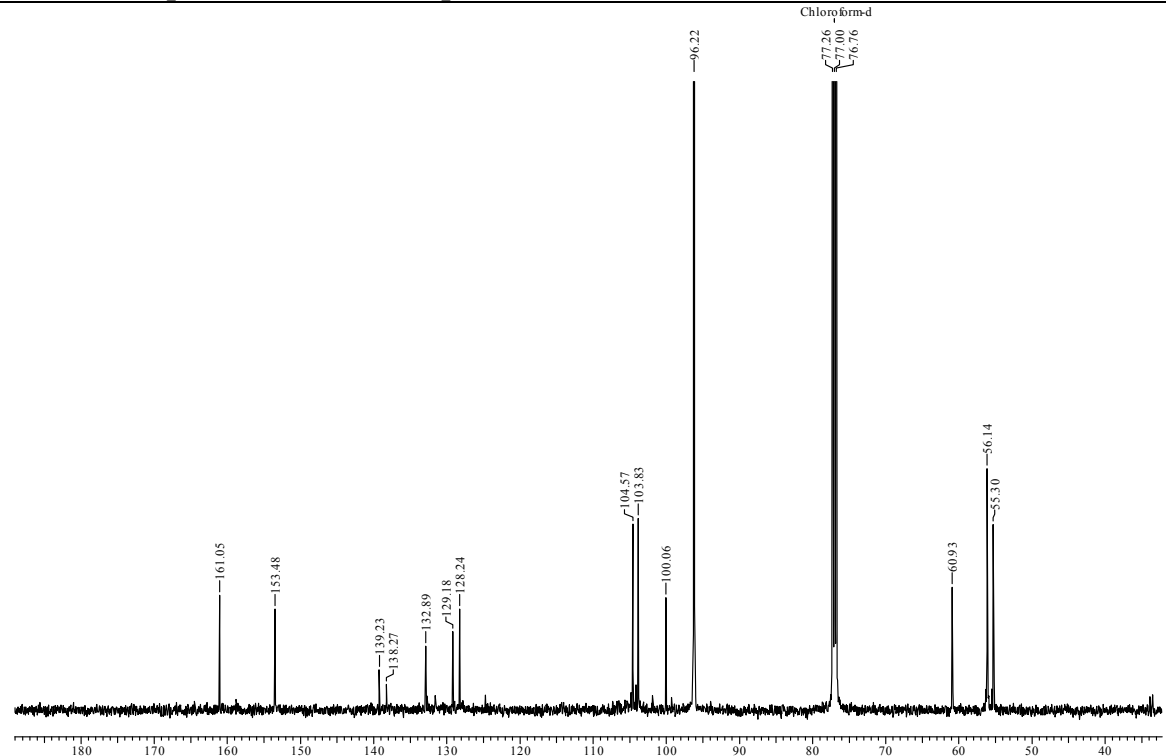
**<sup>13</sup>C NMR Spectrum of the Compound 21 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 100 MHz)**



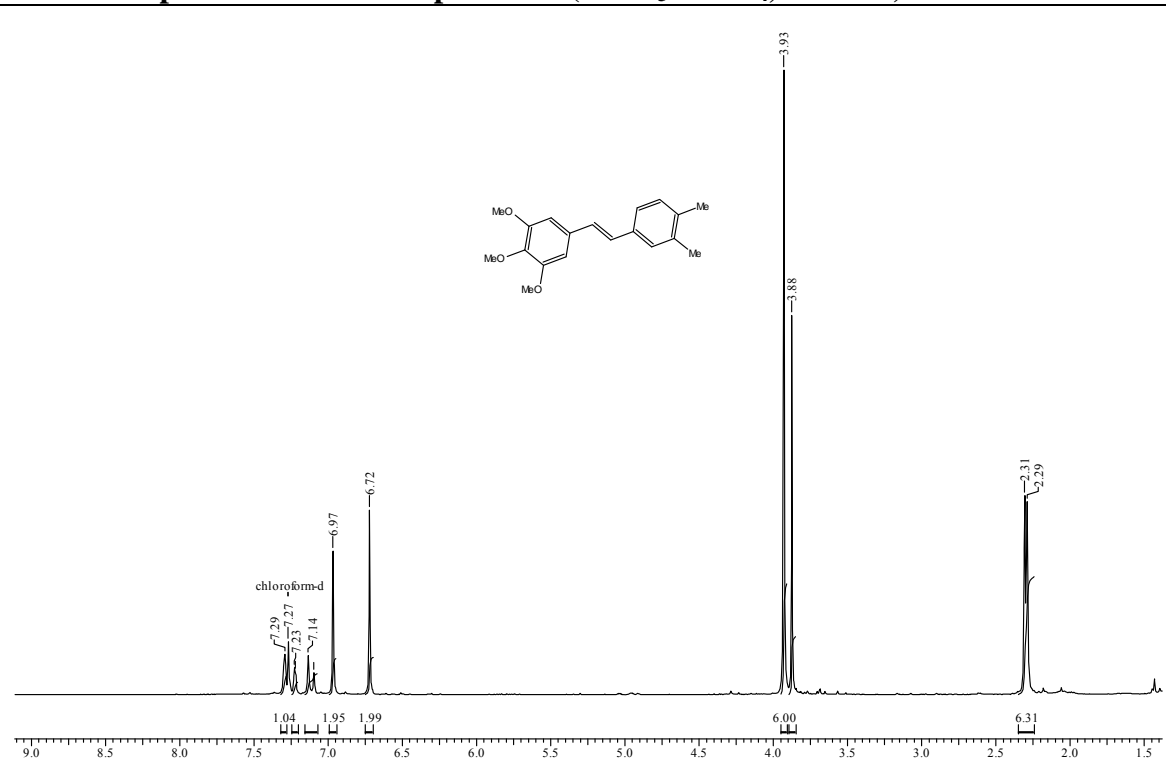
**<sup>1</sup>H NMR Spectrum of the Compound 22 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



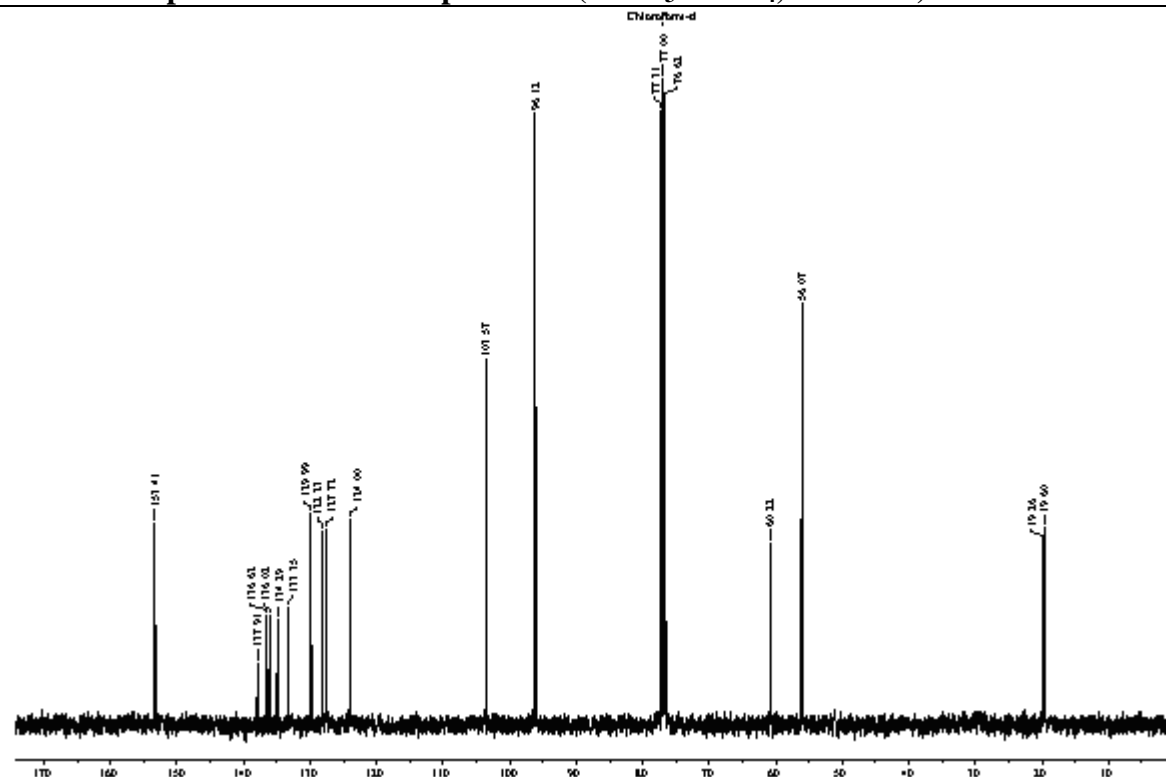
**<sup>13</sup>C NMR Spectrum of the Compound 22 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 100 MHz)**



**<sup>1</sup>H NMR Spectrum of the Compound 23 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 50 MHz)**



**<sup>13</sup>C NMR Spectrum of the Compound 23 (CDCl<sub>3</sub> + CCl<sub>4</sub>, 100 MHz)**



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## **CHAPTER 6**

### **C-C Coupling by the Ullmann Reaction Using Heterogeneous Catalyst**

## CHAPTER-6

# C-C Coupling by the Ullmann Reaction Using Heterogeneous Catalysts

### 6.1 BACKGROUND AND OBJECTIVE OF THE PRESENT WORK

The Ullmann reaction, initially reported in 1901[1], has long been employed by chemists to generate a C-C bond between two aromatic nuclei. Typically the Ullmann reaction is an important tool for generating the C-C bond between aryl halide (two molecular equivalent) in the presence of one equivalent of finely divided copper at high temperature (above 170 °C) with elimination of copper halide for the preparation of symmetrical, unsymmetrical biaryls and biphenylenes. Copper is particularly very effective in this type of condensation reaction. This procedure and variants were comprehensively reviewed several decades ago [2 - 4].

The traditional version of the Ullmann reaction requires harsh reaction conditions, and the reaction has a reputation for erratic yields. Since its discovery some improvements and alternative procedures have been introduced. Considerable improvements have been made through the last century. Dimethylformamide is a solvent, which permits the use of lower temperature and a lower proportion of copper. Besides this the use of an activated form of copper powder made by the reduction of copper iodide with potassium, allows the reaction to be carried out at even lower temperatures (about 85 °C) with improved yields. The reaction can be accelerated considerably using ultrasound [5].

The major limitation of the original Ullmann reaction was the formation of only symmetrical biaryls. Several attempts to synthesize unsymmetrical biaryls have been made, and

some success has been achieved by associating aryl halides of different reactivities. These extensions of the original Ullmann reaction to unsymmetrical biaryls formation did however require the use of a large excess of the “activated” aryl.

Recently, a review is published on the use of stoichiometric amounts of copper, nickel, zinc and palladium as a reagent/catalyst [6] where biaryl axis is the central building block in a very large number of natural products of differing structure, biological activity, and biosynthetic origin, including for example polyketides, terpenes, lignans, coumarins, flavonoids, tannins, peptides and alkaloids.

Some other examples of the Ullmann coupling are with zerovalent nickel promoted coupling [7] to form biaryls and first synthesis of Alnusone, novel palladium catalyzed couplings in presence of equimolar amounts of trialkylamine as a co-catalyst [8], homocoupling of aryl halide by palladium acetate and tetra-*n*-butylammonium bromide mixture [9] for the preparation of functionalized biphenyls.

Recently Li et.al. [10] have reported the catalytic amount of 18-crown-6 and zinc mediated reductive coupling of aryl halides catalyzed by palladium on carbon at ambient temperature in water under air atmosphere.

More recently, there is a report on palladium-catalyzed Ullmann-type coupling with zinc in presence of water and liquid carbon dioxide [11], fluorinated palladium catalyzed coupling reaction in supercritical carbon dioxide [12] under solvent less conditions, synthesis of symmetrical functionalized biaryls from aryl halides catalyzed by commercial zinc dust using ammonium formate [13].

One-pot synthesis of symmetrical biaryls [14], where biaryls play an important role in modern organic chemistry like natural products having biological activity, containing

symmetrical or unsymmetrical biaryl units such as Michell amine A or the secalonic acid, has also been reported. There is a report on convenient sonochemical zinc mediated Ullmann homocouplings carried out in aqueous media under CO<sub>2</sub> bubbling in presence of Pd/C [15].

The fact that, the easy catalyst separation, recycling and the potential to increase the existing catalyst activity makes supported Pd catalysts an important alternative to homogeneous catalysts for industrial applications.

This was undertaken to use a heterogeneous catalyst containing palladium on zirconia as a highly environ-friendly efficient catalyst for the Ullmann reaction of aryl halides to biphenyl in good yield; the catalyst can be easily separated and reused.

## **6.2 CATALYSTS AND BRIEF EXPERIMENTAL PROCEDURES**

The zirconia supported Pd catalysts (Pd loading = 2.5 wt. %) were prepared by different methods like impregnation, deposition-precipitation (DP), homogeneous-deposition-precipitation (HDP) and co-precipitation (CP) methods. The procedures of catalyst preparation have already been described in Chapter 2, section 2.2.5. The general experimental procedure for carrying out the Ullmann reaction is given below;

To 5 ml of DMF, were added 2.5 mmol of aryl halide (with or without 2.5 mmol of second aryl halide), catalyst (10 wt % w.r.to aryl halide) and 3.62 mmol of base. The mixture was stirred at 140 °C under nitrogen atmosphere for an appropriate time and the reaction was monitored by TLC. After completion of reaction, the catalyst was separated by filtration and washed with DMF (3 x 3 ml). Then the filtrate was diluted with water followed by extraction with ethyl acetate to give the crude product, which was subsequently purified by column chromatography on silica gel with petroleum ether/ethyl acetate as an eluent. The catalyst was

further washed with acetone, dried and reused. The reaction products were isolated by column chromatography and were confirmed by NMR, IR, MS and elemental analysis.

### 6.3 CHARACTERIZATION OF THE CATALYST

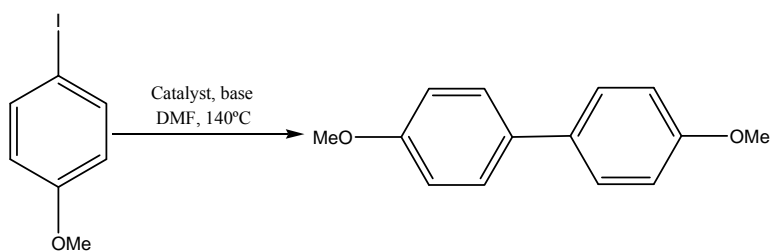
The palladium (2.5 wt %)/zirconia catalyst was characterized by XRD [using a Holland Phillips Diffractometer PW/1730 series X-ray generator with  $\text{CuK}\alpha$  radiations] for their bulk Pd species ( $\text{Pd}^0$  or  $\text{PdO}$ ). Surface area of the catalyst was measured using a Monosorb Surface Area Analyzer (Quantachrome Corp., USA) based on the dynamic adsorption/desorption technique. The catalyst was also characterized by TEM (using a JEOL model 1200EX with CCD camera instrument) for Pd particle size; the sample for TEM studies was prepared by placing a drop of an acetone suspension of the catalyst on a carbon coated copper grid.

The detailed characterization of the catalyst has already been discussed in Chapter 5, section 5.3.6.

### 6.4 RESULTS AND DISCUSSION

#### 6.4.1 Influence of the Catalyst Preparation Methods

In the present study, we have prepared the zirconia supported Pd catalyst by different methods (viz. impregnation, deposition-precipitation, homogeneous-deposition-precipitation



**Scheme 6.1**

and co-precipitation methods). The Ullmann reaction of aryl halides (Scheme 6.1) was carried out using the supported palladium/zirconia catalysts prepared by the different methods and the isolated yields are reported in (Table 6.1) at 140 °C for 15 h.

It is interesting to note that the method of Pd deposition on the support has strong influence on the product yield of Ullmann reaction of aryl halide. Interestingly, the impregnation method produced the best catalyst. This may be due to higher palladium loading

**Table 6.1:** Results of method of Pd/zirconia catalyst preparation on the Ullmann coupling reaction at 140 °C [reaction mixture = 2.5 mmol 4-iodoanisole (with or without 2.5 mmol of second aryl halide) + 3.62 mmol base + 5 ml DMF + catalyst (10 wt % w. r. to 4-iodoanisole)].

Catalyst preparation method	Reaction time (h)	Isolated yield (%)
HDP	8	43
DP	12	37
Co-precipitation	10	16
Impregnation	6	85
Without catalyst	15	5.5

on the support surface thus providing higher catalytic active sites. For the other methods, DP, CP and HDP, the best results were obtained with the catalyst prepared by HDP. The catalysts prepared by HDP also showed good performance because of the expected higher dispersion of Pd on the support and also due to the higher Pd loading as compared to the catalyst prepared by

DP and CP. In all cases, the product formed was mainly 4, 4'-dimethoxybiphenyl. In absence of catalyst, the product yield was only 5.5 %. The best performance in the Ullmann reaction was shown by the Pd/ZrO<sub>2</sub> catalyst prepared by the impregnation method and further studies were carried out using this catalyst.

## **6.4.2 Influence of Different Reaction Parameters in the Ullmann Reaction**

### ***6.4.2.1 Influence of Various Aryl halides***

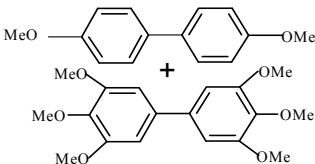
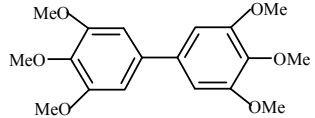
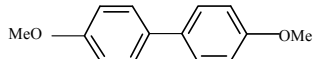
We firstly chose coupling of *p*-iodoanisole (Scheme 6.1) as a model reaction system in the presence of Pd/zirconia (prepared by the impregnation) catalyst and the palladium catalyzed homocoupling protocol that has developed and was applicable to various aryl iodides, as evident from Table 6.2.

Arylation reactions are part of the synthetic route to most substituted biphenyls. These substituted biphenyls are useful monomers for the synthesis of high performance materials. The coupling reaction of both electron-rich and electron-poor aryl iodides worked well. The substrates having a substituent at the para positions reacted particularly well, leading to the corresponding biphenyls in good yields.

As expected aryl bromides were less reactive than aryl iodides under the similar conditions (entry no.5). The catalytic activity, as expected, depends on the aryl halides as well as the substituents on the aryl halide.



**Table 6.2:** Results of Ullmann Coupling of substituted aryl halides over Pd/zirconia catalyst at 140 °C [reaction mixture = 2.5 mmol aryl halide (with or without 2.5 mmol of second aryl halide) + 5 ml DMF + 3.62 mmol Base + catalyst (10 wt% w. r. to aryl halide)].

Entry	Substrates	Reaction Time (h)	Product <sup>a</sup>	Yield (%)
1	<i>p</i> -Iodoanisole	6	4,4'-Dimethoxy-biphenyl	85
2	Iodobenzene	7	Biphenyl	88
3	<i>p</i> -Iodoanisole + 3,4,5-Trimethoxyiodobenzene	5		64 + 25
4	3,4,5-Trimethoxyiodobenzene	5		80
5	<i>P</i> -Bromoanisole	20		46
6	<i>p</i> -Iodoanisole + Iodobenzene	7	4,4'-Dimethoxy-biphenyl + Biphenyl + 4-Methoxy-biphenyl	64 + 21 + 12

<sup>a</sup>The products were characterized by <sup>1</sup>H NMR and IR spectroscopy.

#### 6.4.2.2 Effect of Different Solvents

To check the efficiency of the catalyst and to optimize the reaction conditions, different solvents have been used in the Ullmann coupling of *p*-iodoanisole, under similar reaction conditions. Even though other polar solvents like NMP, ethanol and water can be used, but DMF showed best results with more or less active aryl halides (Table 6.3). The other solvents

like CH<sub>3</sub>CN and xylene gave lower yield and required longer reaction time. However, no reaction was observed with solvents like water, 1, 4-dioxan, toluene and ethanol. Among the different solvents, DMF was found to be the best solvent for providing very good conversion/product yield.

**Table 6.3:** Results of Ullmann coupling of 4-iodoanisole to afford 4, 4'-dimethoxybiphenyl in the presence of different solvents at reflux temperature [reaction conditions = 2.5 mmol 4-iodoanisole + 3.62 mmol K<sub>2</sub>CO<sub>3</sub> + 5 ml solvent + catalyst (10 wt % w. r. to 4-iodoanisole)]

Solvent used	Reaction time (h)	Product yield (%)
DMF	6	85
NMP	10	19
Xylene	12	3
Ethanol, 1, 4-Dioxan.	20	No reaction
Toluene, Water and Acetonitrile	12	14

#### 6.4.2.3 Effect of Different Bases

Among the various bases NaOAc, Na<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub> and zinc dust (inorganic bases) pyridine and Et<sub>3</sub>N (organic bases) screened, K<sub>2</sub>CO<sub>3</sub> was found to be the most effective and convenient base to use for the Ullmann reaction with palladium/zirconia catalyst (Table 6.4).

The other reaction parameters have been optimized using  $K_2CO_3$  as the base. The organic bases triethylamine and pyridine showed poorer performance in the Ullmann reaction.

**Table 6.4:** Results of Ullmann coupling of 4-iodoanisole to afford 4, 4'-dimethoxybiphenyl in the presence of different bases at 140 °C [reaction conditions = 2.5 mmol 4-iodoanisole + 3.62 mmol base + 5 ml DMF + catalyst (10 wt % w. r. to 4-iodoanisole)]

Base used	Reaction time (h)	Product yield (%)
NaOAc	20	25
$Na_2CO_3$	20	20
Triethyl amine	20	10
Pyridine	20	5
Zinc dust	20	30
$K_2CO_3$	6	85

#### 6.4.2.4 Effect of Reaction Temperature

Although the Ullmann coupling of *p*-iodoanisole can be performed even at lower temperatures, the yield of product varies depending upon the temperature. No reaction occurred at 0 °C and 50 °C, however, only 39 % yield obtained at 100 °C. At 140 °C, the product yield was quite high (85 %) (Table 6.5).

**Table 6.5:** Results of Ullmann coupling of 4-iodoanisole to afford 4, 4'-dimethoxybiphenyl at different temperature [reaction conditions = 2.5 mmol 4-iodoanisole + 3.62 mmol K<sub>2</sub>CO<sub>3</sub> + 5 ml DMF + catalyst (10 wt % w. r. to 4-iodoanisole)]

Temperature (°C)	Reaction time (h)	Product yield (%)
0	20	No reaction
50	20	No reaction
100	20	39
140	6	85

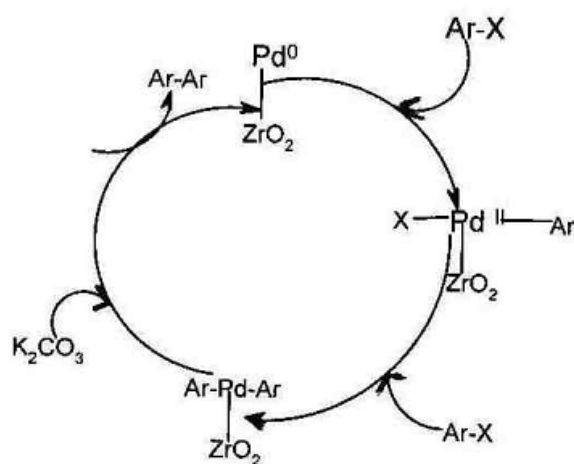
#### 6.4.2.5 Reusability Test of the Catalyst

In order to test the catalyst reusability, the palladium/zirconia catalyst was easily removed from the reaction mixture simply by filtration, washed with DMF first and then acetone, dried and reused in the Ullmann coupling of *p*-iodoanisole at 140 °C. The results showing the reusability of the catalyst are presented in Table 6.6. It is interesting to note that the catalyst showed excellent reusability without significant decrease in the product yield.

**Table 6.6:** Reuse of the Pd/ZrO<sub>2</sub> catalyst in the Ullmann coupling of *p*-iodoanisole at 140 °C [reaction mixture = 2.5 mmol 4-iodoanisole + 0.5 g base + 5 ml DMF + catalyst].

Reuse of Catalyst	Reaction Time (h)	Yield (%)
Reuse I	6	85
Reuse II	6.5	84
Reuse III	7	83
Reuse IV	9	83

It has long been known that the Ullmann reaction of substituted aryl halides results in the formation of biaryl bond only at the carbon atom from which the reactive halogen has been displaced. The possible mechanism of Ullmann coupling of aryl halide over supported palladium catalysts involves in the first step, an oxidative addition of catalyst to the aryl halide to form an activated complex, which then reacts preferentially with the second halide to form the diarylated palladium moiety. Finally, a reductive elimination gives the biaryl product and the palladium (0) species to complete the catalytic cycle, as shown in Scheme 6.2.



**Scheme 6.2.**

## 6.5 CONCLUSIONS

In conclusion, we have developed an efficient method for the Pd/ZrO<sub>2</sub> catalyzed Ullmann-type coupling of aryl halides which provides an operational convenience for the synthesis of biphenyls in good yields. The catalyst showed high activity/selectivity and

excellent reusability. The ease of product separation, safe reaction medium, good yields and low cost of reagents promotes this method as a promising alternative to copper catalyzed Ullmann-type coupling reactions.

The spectral data of some Ullmann reaction products are shown below.

***4, 4'-Dimethoxy-biphenyl***

<sup>1</sup>H NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 50 MHz): δ 7.47 (d, 4H, J=8 Hz), 6.95 (d, 4H, J=8 Hz), 3.85 (s, 6H);

<sup>13</sup>C NMR (CDCl<sub>3</sub>+CCl<sub>4</sub>, 50 MHz): δ 158.7 (2C), 133.5 (2C), 127.7 (4C), 114.2 (4C), 55.2 (2C);

IR (chloroform): 3019, 2957, 1608, 1500, 1215, 1182, 1041, 824 cm<sup>-1</sup>; GC Mass: m/z 214

***Biphenyl***

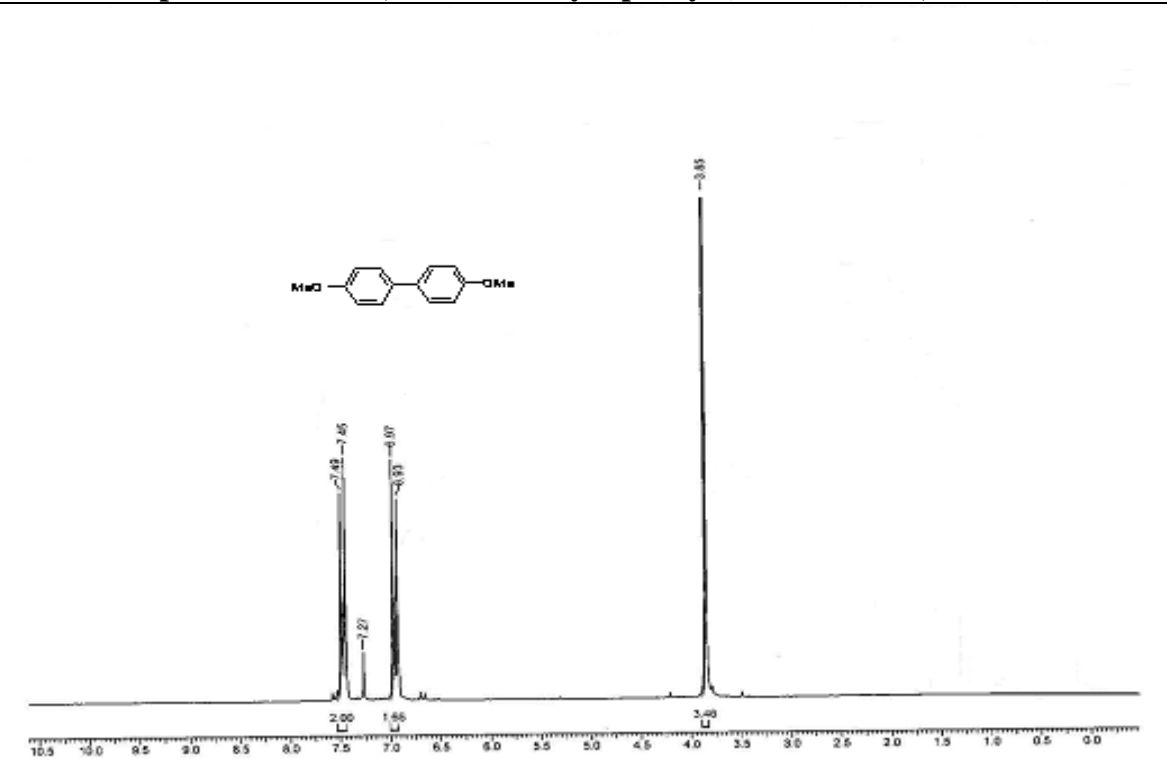
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 50 MHz): δ 7.47 (m, 6H), 7.61 (d, 4H, J = 6 Hz); IR (Neat): 3060, 1638, 1456, 1210, 898, 698, 728 cm<sup>-1</sup>.

***4-Methoxybiphenyl***

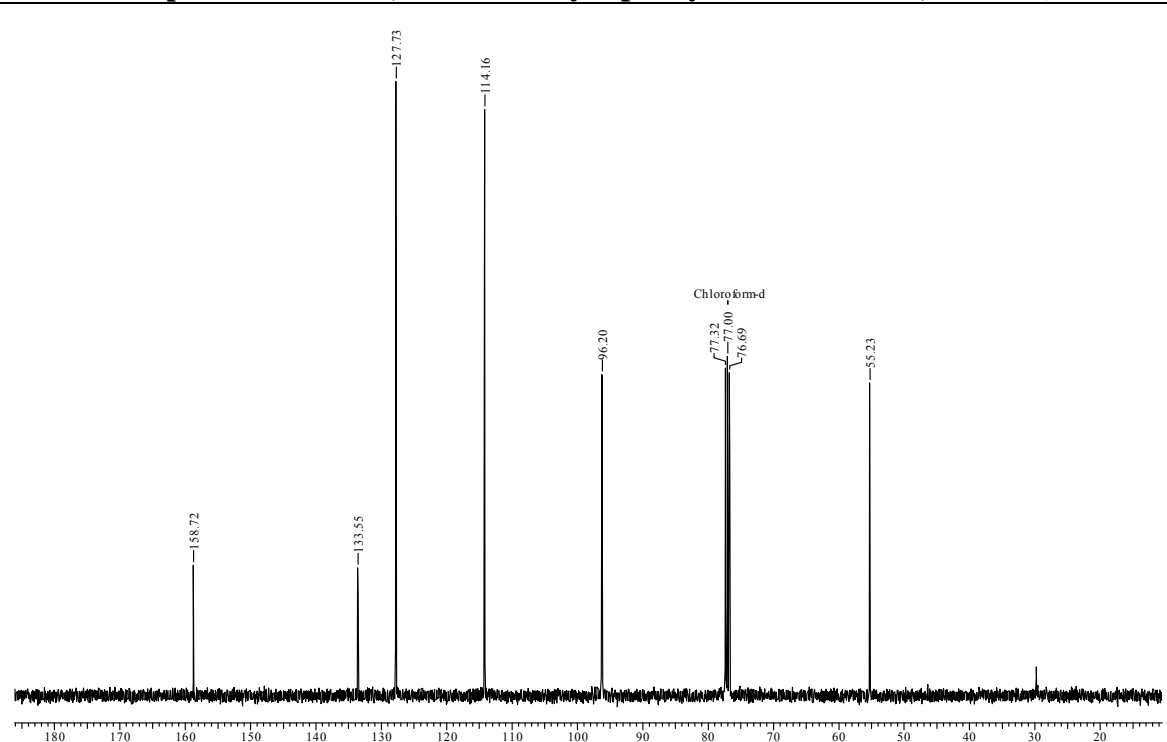
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 50 MHz): δ 7.48 (d, 2H, J=6 Hz), 7.35 (m, 6H), 6.83 (d, 2H, J=6 Hz), 3.73 (s, 3H); IR (chloroform): 2923, 2854, 1606, 1488, 1450, 1251, 1184, 1035, 835, 759, 688 cm<sup>-1</sup>.

## Appendix-6.A

**$^1\text{H}$  NMR Spectrum of the 4,4'-Dimethoxy biphenyl ( $\text{CDCl}_3 + \text{CCl}_4$ , 50 MHz)**



**$^{13}\text{C}$  NMR Spectrum of the 4,4'-Dimethoxy biphenyl ( $\text{CDCl}_3 + \text{CCl}_4$ , 50 MHz)**



## 6.6 REFERENCES

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## PUBLICATIONS BASED ON WORK REPORTED IN THE THESIS

### A. Papers (published/accepted/communicated/to be communicated):

- 1) "Solvent-free selective oxidation of benzyl alcohol and benzaldehyde by tert-Butyl Hydroperoxide using  $\text{MnO}_4^{-1}$ -exchanged Mg-Al-Hydrotalcite Catalysts"  
V. R. Choudhary, **D. K. Dumbre**, V. S. Narkhede and S. K. Jana, *Catal. Lett.*, 86 (2003) 229.
- 2) "Solvent-free oxidation of benzyl alcohol to benzaldehyde by tert-Butyl Hydroperoxide using transition metal containing Layered Double Hydroxides"  
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- 3) "Synthesis of substituted styrenes and stilbenes mediated by palladium on zirconia"  
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- 6) "Solvent-free oxidation of benzyl alcohol to benzaldehyde by tert-Butyl Hydroperoxide using Au/TiO<sub>2</sub> and transition metal oxide supported nanogold catalysts"  
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## PUBLICATIONS OTHER THAN THESIS WORK

### A. Papers (published/accepted/communicated/to be communicated):

- 1) “Efficient *N*-arylation of amines catalyzed by Cu–Fe–hydrotalcite”  
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- 3) “A solvent-free selective oxidation of aldehydes to carboxylic acids by molecular oxygen using MnO<sub>4</sub><sup>-1</sup>-exchanged Mg-Al-Hydrotalcite Catalysts”  
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- 4) “Solvent-free selective oxidation of aldehydes to carboxylic acids by TBHP using MnO<sub>4</sub><sup>-1</sup>-exchanged Mg-Al-Hydrotalcite Catalysts”  
**D. K. Dumbre**, V. H. Tillu and V. R. Choudhary, *Catal. Commun.*, (*To be communicated*).
- 5) Kabachnik–Field synthesis of different  $\alpha$ -aminophosphonates using H-beta zeolites  
V. H. Tillu, **D. K. Dumbre**, R. D. Wakharkar, H. B. Borate and V. R. Choudhary, *Syn. Lett.*, (*To be communicated*).
- 6) Synthesis of phenolsulfonephthalein from phenol and saccharin in Microwave  
V. H. Tillu, **D. K. Dumbre**, R. D. Wakharkar, H. B. Borate and V. R. Choudhary, *Synth. Commun.*, (*To be communicated*).

### PAPER PRESENTED IN SYMPOSIUMS/CONFERENCES

- 1) Design and synthesis of new chemical entities as anticancer agents derived from arylidene tetralones  
V. H. Jadhav, **D. K. Dumbre**, H. B. Borate, R. D. Wakharkar, S. Sarkar, D. Sarkar  
Poster presented in ACS symposium at National Chemical Laboratory, Pune in January 2006.