An-Najah National University
Faculty of Graduate Studies

Recyclable Pd (II) Catalysis on Polymer and Natural Products Supports

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DEDICATION

To my beloved wife Asma'a and my daughter Shayma'a for their inspiration.

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Praise and thanks to Allah, the most merciful for assisting and directing me to the right path, without his help my effort would have gone astray. Special thanks are due to my research supervisor Dr Othman Hamed, for the opportunity to work with him in his research group .I am deeply grateful to him for his constant presence, his willingness to help at any time and his encouragement throughout this research project. Also special thanks are due to Dr Waheed Jondi as the co-supervisor for his continuous assistance and always helping. I also thank the thesis committee, Dr. Waheed Jondi, Dr. Abdullah Walwil, Dr. Nizar Matar and Dr. Mohammad Alnuri for their consent to read my thesis and provide useful suggestions. I would like to take this opportunity to thank the IR. Laboratory manager Mr.Ashraf Salman for his assistance in the matter.

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الإقـــرار

أنا الموقع أدناه مقدم الرسالة التي تحمل العنوان:

Recyclable Pd(II) Catalysis on Polymer and Natural Products Supports

أقر بأن ما اشتملت عليه هذه الرسالة إنما هي نتاج جهدي الخاص، باستثناء ما تمت الإشارة إليه حيثما ورد، وأن هذه الرسالة ككل، أو أي جزء منها لم يقدم من قبل لنيل أية درجة علمية أو بحث علمي أو بحثي لدى أية مؤسسة تعليمية أو بحثية أخرى.

Declaration

The work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

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Date: **التاريخ:**

List of abbreviations

1. OAc: Acetate
2. TMS: Tetramethyl silane
3. DMDI: N,N′-bis{(-)-*cis*-myrtanyl}butylene-2,3-diimine.
4. Curcumin: **[**(E)-1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione].
5. DABCO: Bicyclo [2, 2, 2]-1, 4-diazaoctane.
6. $Eu(hfc)_3$: Tris[3-(heptafluoropropyl-hydroxymethylene)-(+)-camphoratol], Europium(III).
7. PCC: Pyridinium Chlorochromate.
8. THCDBI: TetraHydroCurcuminoids Dibenzylimine.
9. THC: TetraHydroCurcuminoids.
10. THCDI: TetraHydroCurcuminoids Diimine**.**
11. GC: Gas Chromatography.
12. MeOH: Methyl alcohol.
13. BINAP: 2, 2'-bis(diphenylphosphino)-1,1'-binaphthyl.

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Abstract

Three palladium-complexed compounds were prepared and applied successfully in catalyzing many reactions such as Heck and Wacker reactions and also used in carbonylation of olefin. Polymeric polyimine palladium catalyst **12** was prepared from palladium metal immobilized on a polyimine polymer**11**. This polymer was prepared by condensation of a dialdehyde (1,4benzenedicarboxaldehyde **10**) and diamine (ethylene-diamin). Then Palladium metal was introduced on the polymer to give the catalyst. The prepared polymer catalyst was used in synthesis of 2-hydroxy cycloketones and 2-methoxycycloketones as follows: 2-hydroxy cyclohexanone **15** from cyclohexanone, 2-methoxycyclohexanone **31** from cyclohexanone, and α-hydroxy acetophenone **16** from acetophenone. The products were characterized spectroscopicaly using GC, NMR, IR as well as elemental analysis.

The used complex catalyst was reused in the second and third catalytic cycle after washing it with toluene. The reactivity of the catalyst was not diminished in the second and third cycle. However we failed to estimate the percent of Pd remained in the complex after the third usage.

In the second part of this work we prepared two complexes from the cheap starting material Curcumin **6.** Curcumin**,** a natural product, along with two other curcuminoids **7** and **8** were extracted from turmeric. The mixture obtained was 3.57g (11.3% yield). The majority of this yield (88% curcumin) was reduced in the presence of Pd/H_2, to THC **24** which then reacted with 2 equivalents of benzylamine to give THCDBI **25** and then palladium was introduced on it. Pd^{+2} was prepared from oxidation of palladium sponge Pd^0 in the presence of acetonitrile, nitrosonium tetrafluoroborate salt and freshly distilled acetonitrile. The reacture mixture was carried out with stirring under N_2 to give a yellow golden solid. The yellow solid was filtered, washed with hexane, and dried under vacuum. The produced complex Pd (II)-THCDBI **26**, was used to convert cyclopentanone to α-hydroxycyclopentanone **30,** cyclohexanone to 2-hydroxycyclohexanone **15**, 2-methylcyclohexanone to 2-hydroxy-6-methylcyclohexanone **33** and Propiophenone to 2-hydroxypropiophemone **35**. All of the prepared products were characterized spectroscopically using GC, NMR, IR as well as elemental analysis. In the third part, we prepared the last complex which is THCDI-Pd complex **28**. THC **24** was reacted with excess ammonia gas to produce light brown solid in 87% yield which turned out to be Tetrahydrocurcuminoids imine (THCDI) **27.** Compound **27** was analyzed by ^1H and ^{13}C NMR. In the last step of the synthesis, palladium ion Pd^{+2} was introduced into the curcumin-imine compound (THCDI) to form the complex THCDI-Pd **28**. The IR spectral data indicate the presence of Pd in the new complex since the band for C=N dropped by

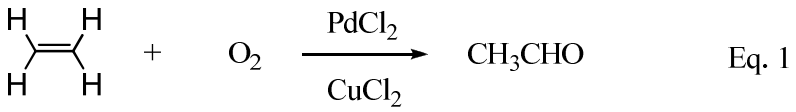
35 cm^{-1}. This drop is due to the formation of Pd-N bond and as a result of back bonding from 4d orbitals of the metal to the empty $*\pi$ of the C=N bond, and so the bond order of C=N decreased causing the IR frequency to shift down. The prepared complex Pd (II)- THCDI **28** was used in the synthesis of 2-hydroxycyclohexanone **15**, 2-hydroxy,6-methyl-cyclohexanone **33**, and 2-hydroxypropiophemone **35**. All of the spectroscopic analysis were in agreement with the results; however, we failed to calculate exactly the amount of Pd metal left in the residue for the polymeric complex. On the other hand we prepared and applied successfully the polymeric complex and hence a recyclable and environmentally friendly complex became possible.

CHAPTER ONE
INTRODUCTION

Background

Transition-metal catalysts are among the most powerful tools for the synthesis of organic molecules. Over the past 50 years, inorganic and organometallic catalysts have been developed for a wide range of transformations and are now common to all scales of productions ranging from the laboratory to the preparation of fine chemicals as well as pharmaceuticals to huge-scale industrial production. The importance of homogeneous transition-metal catalysts has been highlighted through two recent of Nobel Prize winner groups. The first group includes: Sharpless, Noyori, and Knowles who were honored for their enantioselective catalysis in 2001. And the second groups are Chauvin, Grubbs, and Schrock who were cited for olefin metathesis in 2005.

Among the transition metals, palladium occupies a special place in the organic chemist's arsenal because of its ability to catalyze a wide range of reactions. Palladium perhaps first came to standing with commercialization of the Wacker process for the oxidation of ethylene to acetaldehyde in the early 1960s (eq 1). A comprehensive survey of the uses of palladium in organic synthesis through 2000 already, covers over 3400 pages .[1]



Eq. 1

1. Palladium Metal

1.1 History

Palladium was discovered along with rhodium in 1803 by the English chemist William Hyde Wollaston (1766-1828).[2] It was named palladium after the asteroid Pallas, discovered and named by the astronomer Heinrich Wilhelm Olbers two years earlier.[3]

1.2 Physical properties

Palladium is a soft, silver-white metal. It is both malleable, capable of being hammered into thin sheets, and ductile, capable of being drawn into thin wires[4]. The malleability of palladium is similar to that of gold. It can be hammered into sheets to about a millionth of a centimeter thick. An interesting property of palladium is its ability to absorb hydrogen gas like a sponge. When a surface is coated with finely divided palladium metal, the hydrogen gas passes into the space between palladium atoms. Palladium absorbs in up to 900 times its own volume of hydrogen gas.[3,4]

1.3 Chemical properties

Palladium has been called "the least noble" of the noble metals because it is the most reactive among the platinum group. It combines poorly with oxygen under normal conditions but will catch fire if grounded into powder. Palladium does not react with most acids at room temperature but will do so when mixed with most hot acids. Palladium metal also combines with fluorine and chlorine at high temperature. There are five

naturally occurring isotopes of palladium: palladium-102, palladium-105, palladium-106, palladium-108, and palladium-110. The common oxidation states of palladium are 0, +2, and +4. Recently compounds with oxidation state of +6 were synthesized from three molecules of simple Pd(II) complex with two silicon atoms, as shown in Figure1.1.[6]

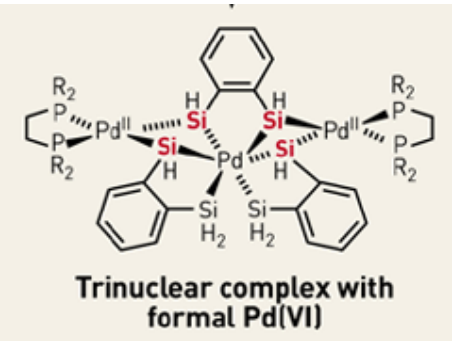


Figure 1.1

1.4 Palladium Catalysts.

Palladium catalysts are one of the most widely used catalysts in the synthesis of pharmaceuticals, cosmetics, and materials worldwide. This could be attributed to several factors: 1) palladium catalysis offer many possibilities of carbon-carbon bond formation; 2) they catalyze wide range of organic functional group transformations ; 3) they are specific and have tolerance to many functional groups such as carbonyl and hydroxyl groups; 4) they are not sensitive to moisture, or even to acid.

The fact that more than ten industrial processes have been developed and are operated based on palladium catalyzed reactions reflects the importance of Pd catalysts commercially.[7,68]

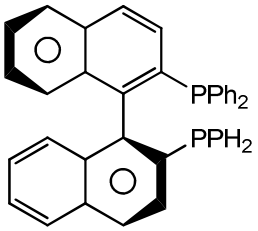
In organic synthesis, two kinds of palladium compounds such as Pd (II) and Pd (0) have been used.[4] Usually Pd (II) is used in stoichiometric amount and Pd (0) in catalytic amount. Pd (II) such as $PdCl_2$ and $Pd(OAc)_2$ are commercially available and widely used in oxidation. Pd (0) when finely divided on carbon, it forms a good catalyst for hydrogenation and dehydrogenation reaction, as well as for petroleum cracking .[2]

Palladium also makes complexes with a wide range of organic ligands ranging from phosphine to Schiff's bases. Among these complexes, the most widely studied are phospine ligands, these include monodentate and multidentate phosphine ligands such as triphenyl phosphine and chiral bidendentate ligand BINAP as shown in Figure1.2. [8]

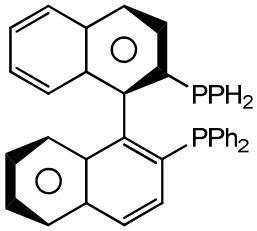
The use of phosphine ligands is necessary for nearly all homogeneous catalysis with precious metals. Phosphine ligands are usually considered strong electron donors and only weak acceptors. The choice of the right ligand can influence 1) the solubility of the active species, 2) the shielding and sterical properties of the catalyst, 3) the electron density at the metal atom, 4) the reactivity of the catalyst in the catalytic cycle, 5) the life time and turnover – numbers of the catalyst, and 6) the enantioselectivity of the reaction with chiral ligands. [9]

Palladium imine complexes are also very important and widely used in palladium chemistry. They play an important role in homogenous catalysis, where the organotransition metal catalyst and reagents are present in the same phase. Furthermore, chiral and achiral Pd(II) complexes

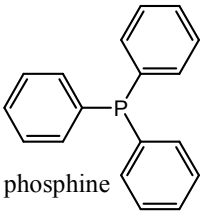
bearing bidentate imine ligands have attracted interest as catalysts for homo- and copolymerization of linear and cyclic olefins with carbon monoxide.[10,11]



(S)-BINAP



(R)-BINAP



Triphenyl phosphine

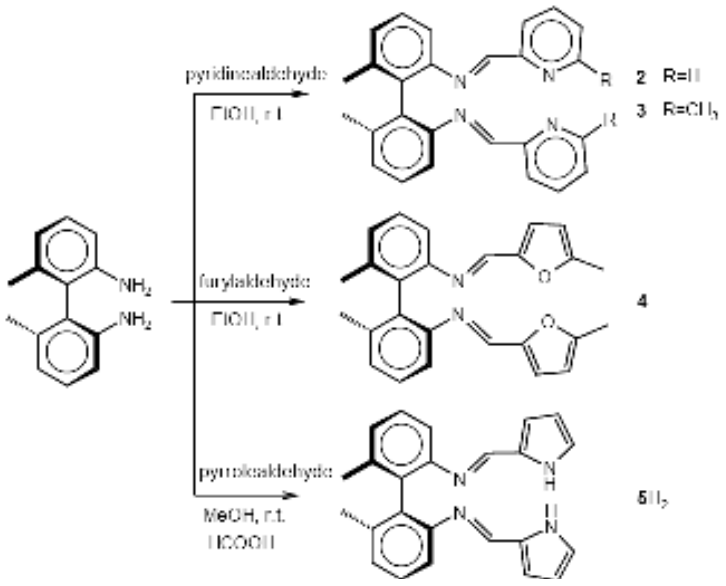
Figure 1.2

1.5. Palladium –Imine Complexes

1. 5. 1. Synthesis of Imine ligands

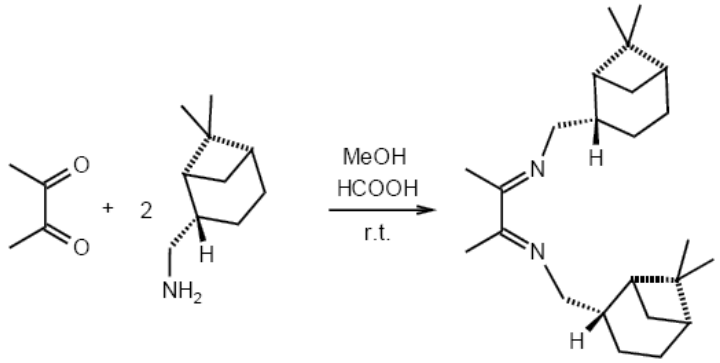
Among other important ligands for palladium are imines. Imines are not commercially available; they are usually prepared from the condensation of carbonyl compounds such as ketones or aldehydes, as well as from amines, often aromatic amines. Scheme1.1 summarizes the synthesis of some reported imine ligands.[12,68] When imine is made by this method, water is produced as a by-product. Since this imine-forming-reaction is usually considered to be revesible reaction, hence water is needed to be removed as it is formed. This is accomplished by distillation, preferably azeotropic distillation, or through hydrate formation using a drying agent such as magnesium sulfate.[13]

Scheme 1.1



Alternative routes for the synthesis of imine ligands have been introduced. In this method a Lewis acid is used as a catalyst. [14] For example when two equivalents of (1R)-(+)-camphor are refluxed with a 1,2-diamine and an excess base such as triethylamine in the presence of $TiCl_4$ for two days, the corresponding diimine is produced in a moderate yield.[15] Nevertheless, in some cases, such as condensing 2,3-butandione with chiral myrtanylamine, over 50% yield was achieved. This condensation was carried out in methanol and the formic acid catalyst whil stirring at ambient- temperature (Scheme 1.2). Precipitation of the diimine product DMDI, N,N-bis{(-)-*cis*-myrtanyl}butylene-2,3-diimine **1**,is the driving force here.

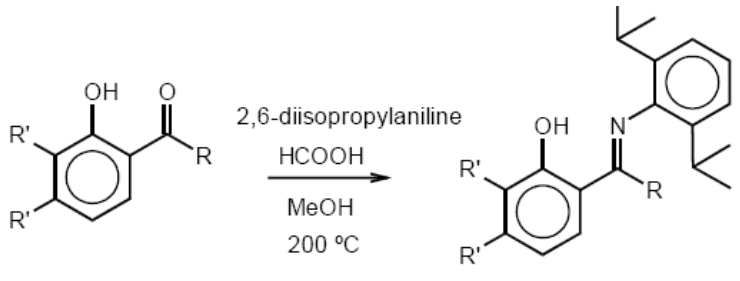
Scheme 1.2



1 (BMDI)

Usually, condensation of aromatic ketones or aldehydes with sterically hindered amines requires severe reaction conditions. For example, condensation of salicylaldehydes with substituted phenyl amines such as 2,6-dialkyl derivatives gave no product. However, when the reaction is carried out at 200 ^{o}C in a closed steel autoclave in the presence of Na_2SO_4 and a catalytic amount of formic acid (Scheme1.3) imine ligands **3** and **4** were isolated in a moderate yield (50%), while ligand **5** was isolated in only 6% yield. No increase of the yield was achieved by varying acid catalyst or solvent or by performing the reaction without solvent and at different temperatures.[10]

Scheme1.3



3 R = CH_3 and R`, R` = H
4 R = CH_3 and R`, R` = 5,6-benzo
5 R = Ph and R`, R` = H

As shown above simple reaction conditions and easy product purification combined with easy availability of a wide spectrum of starting materials may give the chemist a fast entrance to imine ligands.

1.6 Synthesis of Palladium (II) Imine Complexes

Imine ligands contain lone pair of electrons on the nitrogen atom, which is used for the coordination of imine to give a stable complex.

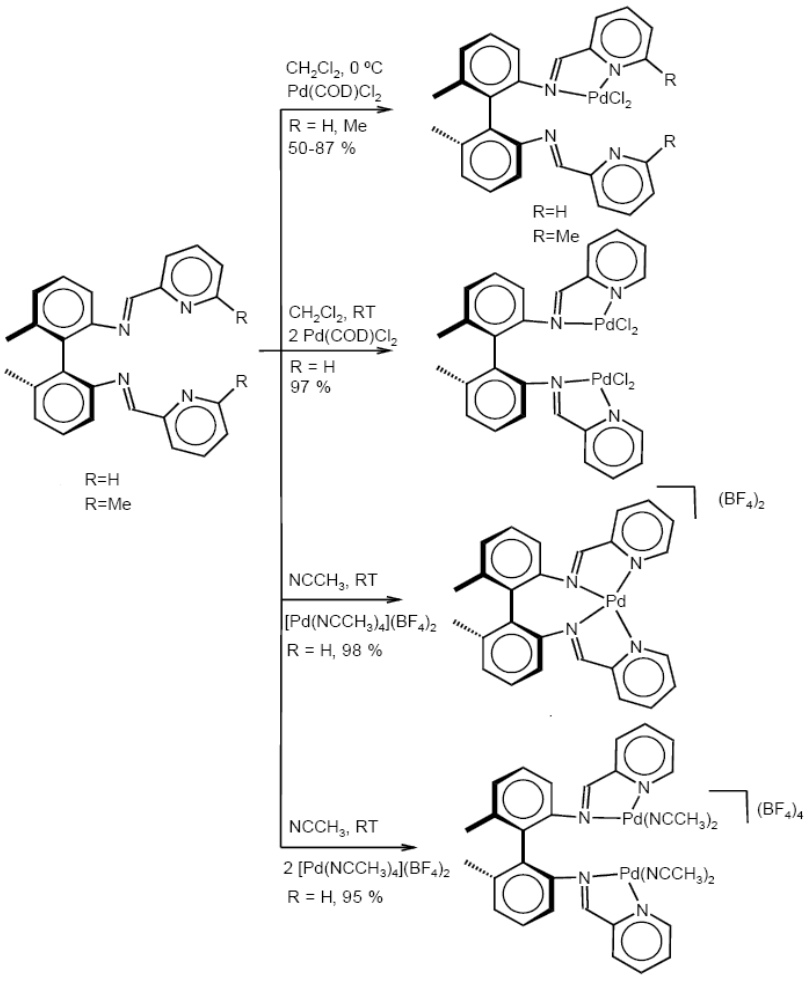
Imine- transition metal complexes are often prepared in two steps: first is the synthesis of imine and then synthesis of the metal- imine complex. Many complexes of imines and palladium (scheme1.4) have been reported in literature.

Transition metal - phosphine ligands complex have been extensively studied in catalytic processes. Catalysts containing nitrogen ligands (imines and amines) are also suitable for many of these processes. These include C-C cross-coupling reaction, hydrogenation, oxidation, allylic alkylation and the Heck reaction. Catalysts bearing nitrogen ligands may perform even better than those with weak Lewis-base phosphorus ligands.[16] Although phosphine transition metal complex still play the main role in industrial applications, nitrogen ligands catalysts are mostly of considerable interest.[17]

Schiff-base imine ligands have played an essential role in the development of transition metal complexes for biological applications, catalysis and materials science.[18] Furthermore, chiral and achiral Pd(II)

complexes bearing bidentate nitrogen donors have attracted interest as catalysts for homo- and hetro- copolymerization of linear and cyclic olefins with carbon monoxide [10,11,19]and for polymerization of functionalized olefins.[20]

Scheme 1.4



The attractiveness of nitrogen donors is enhanced by their good availability.[21] For example, the chiral and achiral multidentate ligands have been applied in transition metal-catalyzed reactions such as enantioselective C-C bond forming reactions,[22] allylic alkylation,[23] oxidation,[24] reduction,[25] and carbonylation of alkenes.[26]

As mentioned above, late transition metal complexes with nitrogen-based ligands have found a wide range of applications in homogeneous catalysis.[17A]

For example, dendimeric pyridylimine-Pd (II) complexes and binuclear Pd (II) complexes with long aliphatic spacers have recently been described as effective catalyst precursors for Heck coupling [27] and ethene polymerization, respectively.[28] Moreover, palladium complexes with chiral bidentate bis(oxazoline) ligands have been found efficient in asymmetric allylic alkylation.[23] Palladium-catalyzed enantioselective transformations have recently been reviewed.[29]

1.7 Polymer supported catalysts.

Currently we are seeing major effort in academic and industrial research devoted to the development of environmentally friendly catalytic tools (Green Chemistry). We are also seeing innovative ideas to solve many of the problems associated with the solution phase in organic synthesis. Among of these, are polymer supported catalysts, these kinds of catalysts offer great advantage over traditional homogenous catalysts since they afford better activity, easy product purification, and catalyst recycling. So after the reaction is complete, catalyst could be filtered, washed off, and re-used.[33-36]

In polymer supported catalysts, the catalytically active species are immobilized on polymer surface through chemical bonds or weaker

interactions such as electron- donor–acceptor interaction or hydrogen bonds.

Palladium catalyst was chosen for the current study because it forms the basis of many hydrocarbon oxidation catalysts.[37,38] Despite that, limited number of examples on polymer supported palladium catalysts are available in this area of research. In one example $PdCl_2$ has been supported on a styrene-divinylbenzene copolymer resin containing $–CH_2N(CH_3)_2$ groups.[39,40] This catalyst is reported to be effective in converting ethylene, dioxygen, and acetic acid to vinyl acetate along with acetaldehyde and ethylene oxide. More recently an organic quinone polymer containing sulphonic acid groups has been used to support palladium (II), yielding a catalyst effective for the conversion of ethylene to acetaldehyde.[41]

A related Wacker-type supported catalyst has also been reported.[42] The support in this case was an oligo-p-phenyleneterephthalamide $(NHPhNHCOPhCO)_n$, presumably chosen for its thermal stability. The supported catalyst was prepared by wet, impregnation of the polymer with a water-acetic acid solution (9: l) of $Pd(OAc)_2$ at room temperature.

After drying, the temperature of the impregnate was raised to 950°C until all volatiles were removed. It is not clear therefore what the final molecular structure of the active catalyst really is.

In another related example resins with phosphine functional groups as those shown in Figure 1.3 have been used in the immobilization of

several palladium complexes and used as a heterogeneous catalysts in Heck and Suzukin-Miyaura reactions. [43] In some of these reactions the recovered catalysts were reported to retain activity over repeated experiments. However these catalysts are limited to fairly activated ArX (X = I, Br, OTf). Several attempts were made to enhance the recyclability of the catalyst.[44]

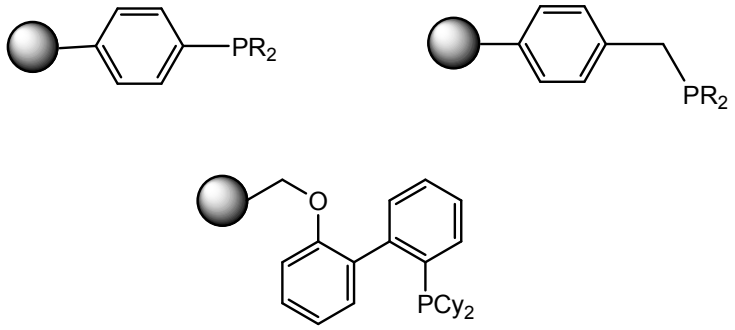


Figure 1.3

1.8 Curcumin

Curcumin **6,** (E)-1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione (Figure1.4) is the major constituent of the yellow pigments isolated from rhizome of Curcuma longa (turmeric). The root of this plant has been used in India as preservative, colorant, flavoring in meals (curry) and as a traditional medicine. One aspect of the most significant finding in medicine is that the four most frequent neoplasias– colon, breast, prostate and lung – are less frequent in India, where this ingredient is widely used). It is known that compound **6** acts as an antioxidant[45], antiinflammatory[46], antitumoral [47] and antiangiogenic [48] which explains the growing interest in this material. It has been established

that **6** is capable of blocking the development of melanoma[49] and that it can correct the genetic mutation that causes cystic fibrosis.[50]

The main components of turmeric are curcumin **6**, demethoxycurcumin **7**, and bisdemethoxycurcumin **8**.[51]The three components together referred to as curcuminoids. The structures of curcuminoids were determined in 1910, they have unique structures because they incorporate several main functional groups such as: the aromatic ring systems in the form of methoxylated phenols.[52] The two carbonyl groups form a diketone, the enol of the heptadiene-3,5-diketone , and two unsaturated carbonyls.

The diketones tautomerize to enols or are easily deprotonated to form enolate ion while unsaturated carbonyl is a good Michael acceptor and undergoes nucleophilic addition.[53] The Michael addition is one of the most important C-C bond – forming reaction in solution-phase organic synthesis. In general, Michael addition reactions are conjugate 1,4-additions of enolates or amines to α, β -unsaturated carbonyl compounds carried out under basic conditions. The enol form (Figure 1.4) is expected to be more energetically stable in both the solid phase and in solution.[51]

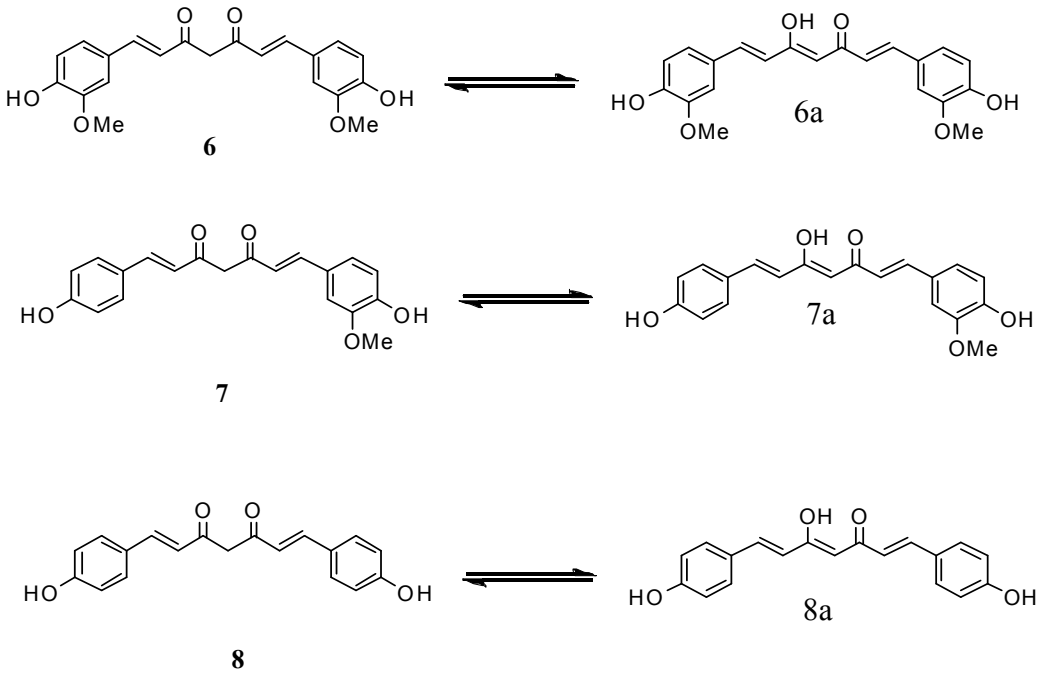


Figure 1.4

Curcumin can bind with heavy metals such as cadmium and lead, which leads to the reduction of their.[54] Also it's quite insoluble in non-polar solvents such as hexane.[55] As mentioned earlier, curcumin is a natural product that can be obtained easily by extraction from plants.

1.9 Aims of the Thesis

The aim of the present work is to design and develop palladium complexes with nitrogen-based ligands and use them to improve existing palladium-catalyzed reactions. The reactions may include but not limited to carbonylation, methoxylation, and hydroxylation of ketones.

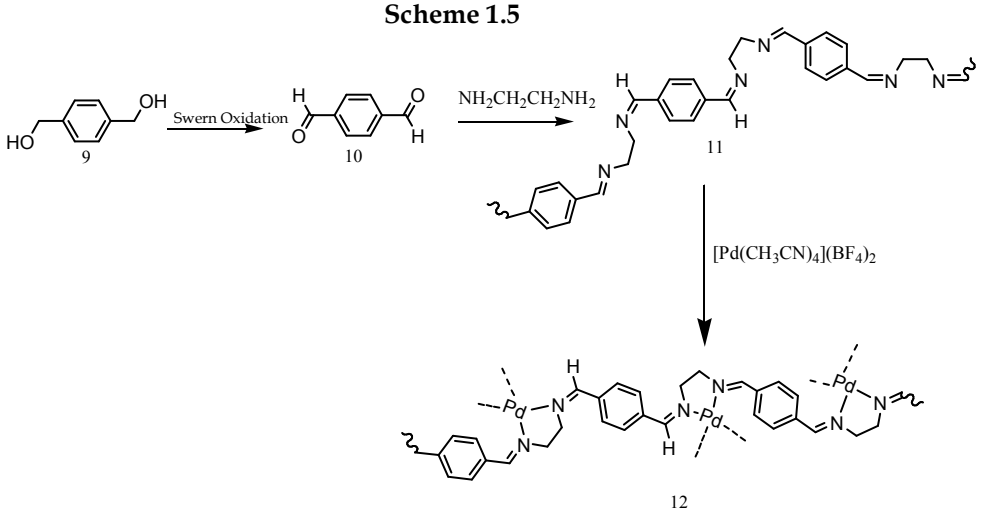
Two different types of ligands were chosen for this purpose:

1. Polymeric polyimine ligands.

2. Natural products based polyamines ligands.

Polymeric polyimine could be prepared by the condensation of 1,4-dibenzaldehyde **(10)** and ethyelendiamine as shown in scheme 1.5. This kind of condensation, as mentioned earlier, is simple and effective tool for the synthesis of imine ligands. The ease of the reaction's work up and purification of the product, combined with the availability of the starting materials made imine ligand our first choice to attain the objective of this work. Palladium (II) then will be introduced onto the polymer chain by reacting polymeric polyimine with tetrakis (acetonitrile) palladium (II) tetra-fluoroborate. As shown in scheme 1.5 the polymeric supported catalyst is novel due to the fact that each polymeric chain carries a multi-catalytic sites, where number of catalytic sites equal number of repeat units.

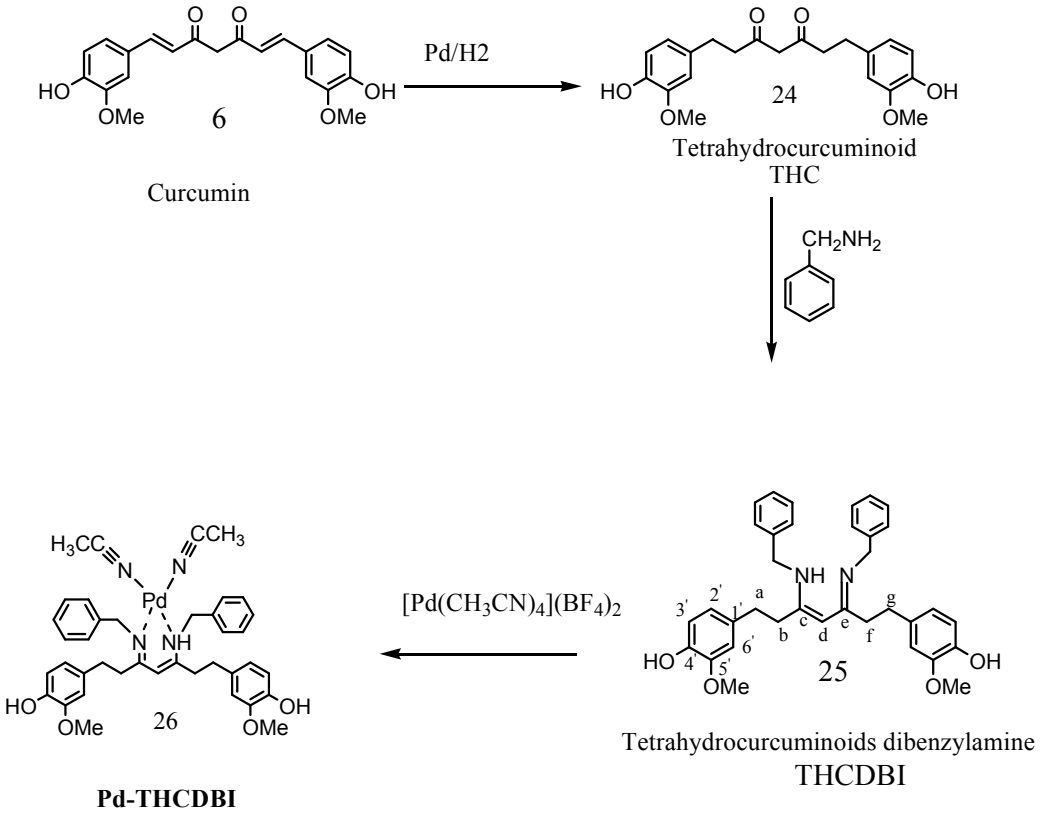
Scheme 1.5



Imine ligands based on natural products were chosen because they could be made easily from natural products and because of their availability as optically active materials. Being optically active may give them uniqueness in the synthesis of optically active transition metal catalysts.

The natural product curcumin was chosen for this work because of its uniqueness in having 1, 3-diketone functionality. These carbonyls make them easy target in converting them into imine derivatives then complexed to palladium (II) as shown in scheme 1.6.

Scheme 1.6



The catalytic activity of the produced complex will be evaluated as mentioned in the previous reactions. The catalytic activity of both systems polymeric polyimine ligands, and curcumin based polyamines toward hydroxylation and methoxylation of ketone will be studied.

It is believed that ligands and their palladium complexes are new to science, and hence many future study and investigations are necessary.

CHAPTER TWO
EXPERIMENTAL

General Experimental

All chemicals were purchased from Aldrich Chemical Company and used without any further purification unless otherwise stated. All new compounds were characterized by ^{1}H NMR, ^{13}C -NMR, and IR spectroscopy, Nuclear Magnetic Resonance (spectra were recorded on **a** Varian VXR Gemini 2000, 300 MHz instrument). All ^{1}H NMR experiments are reported in δ units, (ppm) downfield from tetramethylsilane (TMS). All ^{13}C NMR spectra are reported in ppm relative to the signal of the deuterated chloroform (77.0 ppm). Infrared spectra were recorded on Perkin Elmer Model 1310 Infrared spectrometer or on ATI Mattson Genesis FT-IR spectrometer. Melting points were recorded by Mel-Temp apparatus using a calibrated thermometer. Elemental analyses were performed by An-Najah chemistry department laboratories.

Column chromatography was performed with silica gel (230-400 mesh). Dichloromethane, diethyl ether, tetrahydrofuran, and acetonitrile were used as eluents, dried over calcium hydride (CaH_2), distilled and stored under argon.

All reaction vessels were dried overnight at 110 °C before use. All the solid products were reserved in desiccators.

The % enantiomeric execs (ee) was determined by using ^{1}H NMR in the presence of chiral tris [3-(heptafluoropropyl-hydroxymethylene)-(+)-

camphoratol], europium (III) ($Eu(hfc)_3$). Arange of 0.1-0.3 mole ratio of ($Eu(hfc)_3$) derivative to the chiral material was used.

2.1 Palladium polyimine complex (12)

The complex was prepared in three steps. Initially, the polyimine complex was prepared in two steps, and then palladium was introduced into the complex as indicated in the procedure below.

2.1.1 Preparation of pyridinium chlorochromate (PCC)

To an aqueous solution of HCl (46.0 ml of 6M) in a 250 mL round - bottomed flask, CrO_3 (25.0 g, 0.25mol) was added rapidly with stirring over a period of 5 minutes, cooled in an ice bath, and then pyridine (16.3ml, 0.2mol) was added dropwise with stirring. During the addition a yellow-orange solid appears. After the addition was completed, the mixture was continued to cool down for another 10 min until a precipitate was formed. The solid was collected by suction filtration on centered- glass funnel and dried in vacuum at about 60°C.

2.1.2 Preparation of 1,4 Benzenedicarboxaldehyde (10)

Pyridinium chlorochromate (PCC) (12.9 g, 0.04mol) was suspended in 50 ml dichloromethane in a 250mL round - bottomed flask (250 ml) fitted with a reflux condenser and magnetic stirrer bar. After stirring the mixture for few minutes, 1,4 benzenedimethanol **(9)** (2.76 g, 0.02 mol) dissolved in dichloromethane (10) ml was added in three equal portions and stirred for 2 hours. The black gummy product was filtered, washed with

ether (3 x 20 mL), and then the combined filtrate and ether mixture was dried over $MgSO_4$, filtered, and the ether removed under reduced pressure using a rotary vaporator. The solid residue was re-crystallized from hexane. Melting point of the produced solid **(10)** was 112-114 C°. (Literature m.p for 1,4-benzenedicarbozaldehyde is 114C°)[56], 62% Yield. The IR main band at (1695cm^{-1}) was recorded for the presence of aldehydic C=O. and two bands at 2850 cm^{-1} and 2950 cm^{-1} for the aldehydic hydrogen's indicating the production of terphathaldicarboxaldehyde (10).

2.1.3 Preparation of polyimine (11)

The aldehyde prepared in the previous part, 1,4-benzenedicarboxaldehyde was used to prepare the polyimine, the procedure was repeated several times by two methods.

Method A: **In presence of $MgSO_4$**

To a three neck round-bottomed flask fitted with a condenser equipped with an additional funnel and magnetic stirrer, dichloromethane (20 mL), 1,4-benzendicarboxyladehyde (0.5g, 3.6 mmol) and magnesium sulfate (4.0g) were added. A solution of ethyelendiamine 0.24 ml (8.8 mmol) in dichloromethane (5.0 mL) was added to the mixture dropwise through the additional funnel over a period of 15 minutes then refluxed for two hours. The reaction progress was monitored by TLC using petroleum ether: ethyl acetate (85:15) as an eluant. The reaction mixture was filtered to remove magnesium sulfate and the solvent removed in vacuo.

Petroleum ether (20 ml) was added to the produced milky solution and the produced white precipitate product was collected by suction filtration, washed three times with hexane, and dried in oven at 60 °C. Yield was 0.53 g (93%).

Method B: **Without $MgSO_4$.**

To a three-necked round-bottomed flask fitted with a condenser equipped with an additional funnel and magnetic stirrer, dichloromethane (20mL) and 1,4-benzendicarboxyladehyde (0.5 g, 3.6 mmol) were added. A solution of ethyelendiamine 0.24 ml (8.8 mmol) in dichloromethane (5.0 mL) was added to the mixture dropwise through the additional funnel over a period of 15 minutes then refluxed for two hours. The reaction progress was monitored by TLC using petroleum ether: ethyl acetate (85:15) as an eluent. Petroleum ether (20 ml) was added to the produced milky solution and the produced white precipitate was collected by suction filtration, washed three times with hexane, and dried in oven at 60 °C. Yield was 0.4 g (68%).

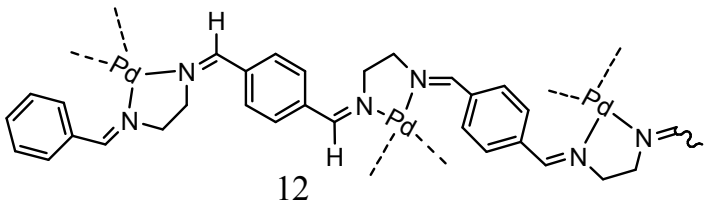
The melting points for the two products were found to be higher than 350 °C. IR spectra gave bands at (1635cm^{-1}) and 3425 cm^{-1} for C=N and N-H bonds respectively (Fig A2 and A3).

2.1.4 Preparation of Tetrakis (acetonitrile) Palladium(II) Tetrafluoroborate.

A flame dried round-bottomed flask under an inert atmosphere (N_2) was charged with palladium (0) sponge (1.0 gram, 0.0094mole), nitrosonium tetrafluoroborate (2.2 g, 0.0188mol) and freshly distilled acetonitrile (30mL). The flask was capped with a rubber septum and stirred under N_2 for about 24 hr (until all Pd sponge disappeared). In the course of the reaction the generated NO was removed periodically. The solvent was removed from the pale yellow solution in vacuo using the rotary evaporator. Diethyl ether (20mL) was added to the oily residue; and the pale yellow solid was collected and dried under vacuum. Yield was 4.0 g (96%).

2.1.5 Preparation of Palladium polymeric polyimine complex(12).

Generally, Pd(II)complexes are prepared by dissolving Tetrakis(acetonitrile) palladium (II) Tetrafluoroborate and the ligand in the proper solvent and leaving the mixture to react at room temperature for 24 hours. Produced solid material is then filtered and washed with diethyl ether or hexane. IR spectrum (Fig A9) showed bands at: 1643cm-^{1} for C=N bond.



12

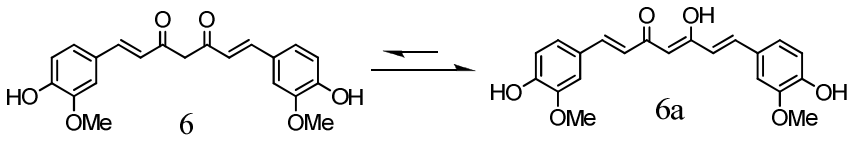
Pd- Polyimine complex

2.2 Palladium (II) -THCDBI complex (26)

The complex was prepared in several steps. First Curcuminoids were extracted from the curcumin and reduced by Pd/H_2 .The product was reacted with two equivalents of benzylamine to produce THCDBI and then palladium was introduced into the complex. A detailed procedure for the preparation of this complex is shown below.

2.2.1 Extraction of Curcuminoids from Turmeric (6)

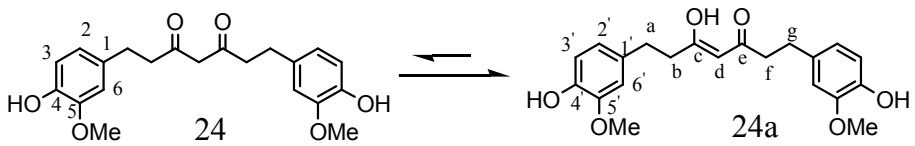
Curcuma longa powder (20.0 g) was suspended in 300 ml ethanol and stirred vigorously for about 24.0 hours at $30C^{o}$. The mixture was filtered and ethanol was removed under vacuum. The yellow gummy residue (containing curcuminoids) was subjected to purification on silica (230–400 mesh) by flash chromatography. The first fraction was eluted with hexane-ethyl acetate (9:1), then ethyl acetate-hexane (6:4), and then methanol-ethyl acetate (1:9) was used to elute the second fraction. Evaporation of the solvent form the first fraction provided an oily material, while the second fraction afforded about 3.57 g (11.9%) of yellow-orange solid. NMR and IR spectra showed that the yellow solid is a mixture of curcuminoids **6, 7** and **8**. But the predominant was compound **6** in 88% yield. ^{1}H NMR (300 MHz) ($CDCl_3$-DMSO- d6) (8:2): δ= 9.45 (broad, 1H, OH vinylic), 7.45-7.55 (m, 2H), 7.25 (d, 1H), 7.05 (dd, 1H), 6.85 (m, 2H), 6.7 (d, 2H), 5.9 (s, 1H) 3.85 (s, 6H). ^{13}C NMR ($CDCl_3$-DMSO-d6) (8:2):δ= 184, 149, 148, 140.5, 130, 127, 124, 121, 115, 115.5, 112, 101, 56.



Curcumin

2.2.2 Preparation of Tetrahydrocurcuminoids (THC) (24)

A low pressure reaction bottle was charged with a solution of curcuminoids 5.0 g in absolute ethanol (100 ml) and the catalyst Pd/C (0.3 g). The bottle was attached to the low pressure hydrogenation apparatus and evacuated, and then hydrogen was admitted to a pressure slightly above 3 atm. The contents of the flask were shaken until absorption of hydrogen stopped (about 4 hrs). The catalyst was removed by filtration and ethanol was removed under vacuum to afford 4.6 g (91.8%) of pale yellow gummy material. The gummy material was purified by flash chromatography using ethyl acetate as eluent. The produced THC **24, 24a,** was analyzed by ^{1}H NMR and ^{13}C NMR. ^{1}H NMR (300 MHz) ($CDCl_3$): δ= 6.8 (d, J = 8.24, 2H), 6.62 (d, J = 8.42 =2H), 6.6 (s, 2H), 5.6 (br, 2H, OH), 5.4 (s, 0.75 H, vinylic), 3.90 (s, 0.5H, diketone), 3.85 (s, 6H, OCH_3), 2.9 (t, J = 7.97, 3H), 2.6 (t, J = 7.14, 3H). ^{13}C NMR ($CDCl_3$ d6) δ: 193.2 (Cc and Ce), 144.5 (C4'), 143.9 (C3'), 132.5 (C1'), 120.7 (C6'), 114.3 (C2'), 110.9 (C5'), 99.8 (Cd), 55.8 (OMe), 40.4 (Cb, Cf), 31.1 (Ca, Cg).

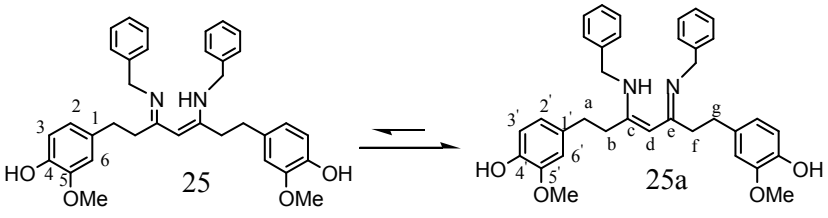


Tetrahydrocurcuminoids

THC

2.2.3 Tetrahydrocurcuminoid dibenzylimine (THCDBI) (25)

Benzylamine (0.64 g, 6.0 mmol) was added to a solution of tetrahydrocurcuminoid **24** (1.10 g 3.0 mmol) in methylene chloride then 5.0 g molecular sieves were added to the mixture. The mixture was stirred at room temperature for about 12 hr, and then gravity filtered to remove molecular sieves. Dichloromethane was removed under reduced pressure and the residue was washed off with hexane to produce brown crystals of Tetrahydrocurcuminoid dibenzylimine, THCDBI, (**25**) in 88% yield. The residue was then washed three times with 30 ml diethyl ether. THCDBI was produced as yellow solid and characterized by. ^{1}H NMR (300 MHz) ($CDCl_3$): δ= 11.3 (br, 0.37H, NH enamine), 7.2-7.45 (m, 16H, arom), 5.6 (br, 2H, OH), 5.3 (s, 0.75 H, vinylic), 3.85 (s, 6H, OCH_3), 2.9 (t, J = 7.97, 4H), 2.6 (t, J = 7.14, 4H). ^{13}C NMR ($CDCl_3$ DMSO-d6) δ: 165.2 (Ce), 158 (Cc), 133 (C1), 122.5 (C2), 115.5 (C3), 144.5 (C4), 147 (C5), 113 (C6), 98.8 (Cd), 56.8 (OMe), 34.5 and 35.6 (Cb, Cf), 30.1 (Ca, Cg).

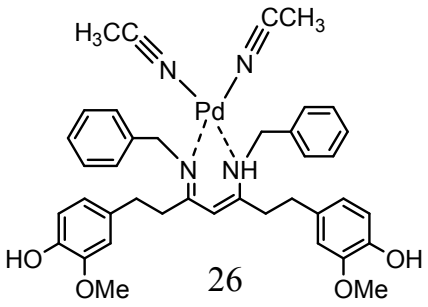


Tetrahydrocurcuminoids dibenzylamine
THCDBI

2.2.4 Preparation of Palladium-THCDBI Complex: (26)

A solution of THCDBI (5.98 g, 11.0 mmol) in methylene chloride (10mL) was added to a solution of tetrakis(acetonitrile)palladium(II)

Tetrafluoroborate (4.44 g, 10 mmol) in methylene chloride (50 .0 mL) under N_2 via a syringe and stirred for 12 hr. The yellow golden solid was filtered, washed off with hexane and dried under vacuum. Elemental analysis showed that complex **26** contains 10.2% of Pd (theoretical value = 14.5%).



26

Pd-THCDBI

2.3. General Procedure for the α-hydroxylation of cycloketones using Pd(II)-THCDBI complex(26).

Palladium-THCDBI complex (0.1 mmoles), CH_3SO_3H (0.47 ml, 0.69 g, 7.0 mmol) and the ketone (11.3 mmol) were added to a solution of $CuCl_2$ (7.7 g, 58.0 mmol) in 30 mL dioxane (40% in water), followed by stirring at room temperature. The progress of the reaction was monitored by GC and TLC. The reaction was interrupted when 50% of the starting material was consumed (48 hrs) and diluted with ether. The produced mixture was stirred at room temperature. The ether layer was separated, washed two times with a solution of sodium bicarbonate 5% (30mL), the ether layer was dried over Na_2SO_4 and concentrated in vacuo. Pure sample of the product was obtained by a preparative GC. Yield was determined by GC.

2.3.1. α-Hydroxylation of Cyclopentanone using Pd (II)-THCDBI complex

Cyclopentanone (11.3 mmol) was used to givehydroxycyclopentanone (**30**), which was purified by column chromatography on silica gel to give 0.81 g (72 %). ^{1}H-NMR and ^{13}C-NMR: δ= 1.66 (1H, s, OH), 1.88-2.38 (m, 6H), 4.10 (t, 1H, J=7.35 Hz) ppm. ^{13}C NMR (100 MHz, CDCl3): δ 19.3, 33.5, 35.1, 58.3, 210.8

2.3.2 α-Hydroxylation of Cyclohexanone using Pd(II)-THCDBI Complex

Cyclohexanone (1.0mL,11.3 mmol) was used to give hydroxycyclohexanone, which was purified by column chromatography on silica gel to give about 0.52 g (47.1%). The product was identified by ^{1}H-NMR and ^{13}C-NMR as 2-hydroxy cyclohexanone (**15**). ^{1}H NMR (300 MHz) ($CDCl_3$): δ = 1.41–1.65 (4H, m), 2.23 (1H, br, OH), 2.21–2.45 (4H, m), 4.13 (1H, q, J = 6.25 Hz,

CH–OH); ^{13}C NMR (300 MHz) ($CDCl_3$): δ = 20.0, 22.8, 26.9, 32.9, 40.9, 75.9, 203.7. FTIR (neat): 3146, 2969, 1790, 1716, 1383, 1097 cm^{-1}.

2.3.3 α-Hydroxylation of 2-methylcyclohexanone using Pd(II)-THCDBI complex

2-Methylcyclohexanone (1.0 mL, 11.3 mmol) was used to give two products 6-methyl-2-hydroxycyclohexanone **(33)** 0.66 g (49%), and its dehydration product 2-methyl, 2-hydroxycyclohexanone. ^{1}H-NMR (300

MHz, CDCl3) for 6-methyl-2-hydroxycyclohexanone:δ = 1.04 (d, 3H, J/6.8 Hz), 1.55 (1H, s, OH), 1.71-1.79 (m, 2H), 2.1 (m, 1H), 2.2 (m, 1H), 2.20-2.30 (m, 2H), 2.56 (dd, 1H, J-5.08, 8.65 Hz), 4.22 (t, 1H, J 7.38 Hz). ^{13}C-NMR (300 MHz, $CDCl_3$): δ = 21.7, 28.1, 33.9, 34.3, 44.9, 60.4, 204.1 ppm. FTIR (neat): 3150, 2973, 1796, 1717, 1383, 1097 cm^{-1}. ^{1}HNM (300 MHz, $CDCl_3$) for 2-methyl cyclohex-2-en-1-one: δ: 1.86 (s, 3H), 1.97 (m, 2H), 2.43 (q, 2H, J= 5.70 Hz), 2.52 (t, 1H, J=7.0 Hz), 5.93 (t, 1H, J4.76 Hz). ^{3}C-NMR (300 MHz, $CDCl_3$): δ= 23.0, 24.4, 38.9, 44.9, 116.3, 151.5, 194.4.

2.3.4 α-Hydroxylation of Propiophenone using Pd (II)- THCDBI complex

Propiophenone (1.15 g, 1.5 mL, 11.3 mmol) was used to give 2-hydroxypropiopheone which was purified by column chromatography on silica gel to give 0.7 g (41 %). The product was characterized by ^{1}H-NMR and ^{13}C-NMR as 2-hydroxypropiophenone **(35)**. ^{1}H NMR (300 MHz) ($CDCl_3$): δ= 7.78 (2H, m), 7.46 (2H, m), 7.6 (1H, m), 4.82 (1H, CH-OH, q), 3.6 (1H, s, OH), 1.52 (3H, d), ^{13}C NMR (300 MHz), ($CDCl_3$): δ = 198.2, 134.0, 132.7, 127.6, 126.5, 71.2, 21.8. FTIR (neat) cm^{-1}: 3146, 3060, 2959, 1730, 1716, 1383, 1097.

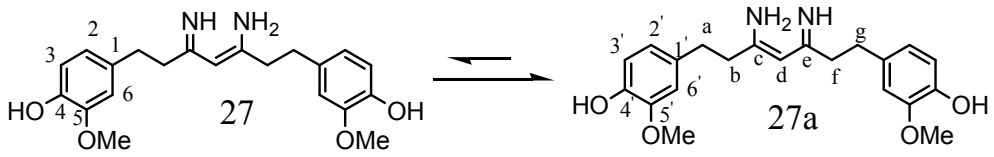
2.4. Preparation of Palladium (II) –Tetrahydrocurcuiminoid diimine (Pd-THCDI) complex (28).

A multi-step reaction was used to prepare Palladium (II)–Tetrahydrocurcuiminoid diimine (THC) **24** which was reacted with excess

ammonia to give Tetrahydrocurcuminoid Diimine THCDI **27** and then palladium was introduced into the complex.

2.4.1 Tetrahydrocurcuminoid Diimine (THCDI) (28).

Excess ammonia gas was bubbled through a solution of Tetrahydrocurcuminoid **24** (1.10 g, 3.0 mmol) in methylene chloride (20 mL) containing molecular sieves (5.0 g). The mixture was stirred at room temperature for about 12 hrs and then filtered off to remove molecular sieves. Dichloromethane was removed under reduced pressure and the residue was washed with hexane to produce brown solid product, which was washed three times with 30 ml diethyl ether. The produced light brown solid was dried under vacuum at 60 °C. The weight of the brown solid product was 0.96 g (2.61 mmol, yield=87%). The product was analyzed by ^{1}H and ^{13}C NMR to be Tetrahydrocurcuminoid diimine **27**. ^{1}H NMR (300 MHz) ($CDCl_3$): δ= 9.8 (s, 1H, =NH), 6.67-6.79 (m, 6H, arom), 5.8 (s, 1H, vinylic), 5.5 (2H, NH_2), 3.85 (s, 6H, OCH_3), 2.5-2.9 (m, 8H). ^{13}C NMR ($CDCl_3$ d6) :δ =164.2 (Ce), 147.3 (Cc), , 144.1 (C4'), 115.5 (C3'), 133.7 (C1'), 114.3 (C6'), 129.5 (C2'), 146.5 (C5'), 55.7 (Cd), 49.6 (OMe), 40.1 (Cb, Cf), 29.7 (Ca, Cg).

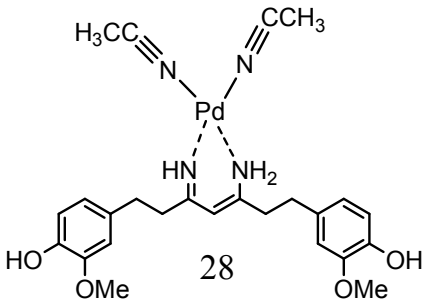


Tetrahydrocurcumindiimine THCDI

(*Z*)-4,4'-(3-amino-5-iminohept-3-ene-1,7-diyl)bis(2-methoxyphenol)

2.4.2 Preparation of Palladium-THCDI Complex: (28)

A solution of THCDI (4.03 g, 11.0 mmol) in methylene chloride (10 mL) was added to a solution of (tetrakis (acetonitrile) palladium (II) tetrafluoroborate) (4.44 g,10 mmol) in methylene chloride (20 mL) under N_2 via a syringe and stirred for 12 hr. The yellow golden solid was gravity filtered, washed off with hexane and dried under vacuum. Elemental analysis showed that complex **28** contains 12.3% of Pd (theoretical value = 14.5%).



28

Pd-THCDI

2.5 General Procedure for the α-hydroxylation of cycloketones using Pd(II)-THCDI complex

Palladium-THCDI complex **28** (0.103 mmoles), CH_3SO_3H (0.47 ml, 0.69 g, 7.0 mmol) and the ketone (11.3 mmol) were added to a solution of $CuCl_2$ (7.7 g, 58.0 mmol) in 30 mL dioxane (contains 10% water). The mixture was stirred at room temperature under a positive pressure of oxygen. The progress of the reaction was monitored by GC and TLC. The reaction was interrupted when 50% of the starting material was consumed (48 hrs) and diluted with ether. The ether layer was separated, washed two

times with a solution of sodium bicarbonate 5% (30mL), the ether layer was dried over Na_2SO_4 and concentrated in vacuo. Pure sample of the product was obtained by a preparative GC. The yield was determined by GC.

2.5.1 α-Hydroxylation of cyclohexanone using Pd (II)- THCDI complex

Cyclohexanone (1.0 mL, 11.3 mmol) was used in this reaction. Pure sample of the product was obtained by column chromatography on silica gel to afford 0.4 g (yield 37.5%). The product was identified by ^{1}H-NMR and ^{13}C-NMR as 2-hydroxycyclopentanone.

2.5.2 α-Hydroxylation of 2-methylcyclohexanone using Pd (II)- THCDI complex

2-Methylcyclohexanone (1.0 mL, 11.3 mmol) was used in this reaction. Two products were separated 2-hydroxy,6-methyl-cyclohexanone, and its dehydration product 2-methylcyclohex-2-en-1-one. The main product was 2-hydroxy, 6-methyl-cyclohexanone, 0.50 (yield 36.5%. ^{1}H- and ^{13}C-NMR identified the products respectively.

2.5.3 α-Hydroxylation of Propiophenone using Pd (II)- THCDI complex

Propiophenone **(34)** (1.15 g, 1.5 mL, 11.3 mmol) was used in this reaction. Pure sample of the product was obtained by column chromatography on silica gel to afford about 1.08 g (32%). The product was identified by ^{1}H-NMR and ^{13}C-NMR as 2-hydroxypropiophenone

(35)[1.] H NMR (300 MHz), (CDCl3): δ= 7.78 (2H, m), 7.46 (2H, m), 7.6 (1H, m), 4.82 (1H, CH-OH, q), 3.6 (1H, s, OH), 1.52 (3H, d), ^{13}C NMR (300 MHz), ($CDCl_3$): δ = 198.2, 134.0, 132.7, 127.6, 126.5, 71.2, 21.8. FTIR (neat): 3146, 3060, 2959, 1730, 1716, 1383, 1097 cm^{-1}

2.6 General procedure for the α-hydroxylation of cycloketones using palladium polymeric polyimine complex

Palladium-polymeric polyimine complex (0.103 g), CH_3SO_3H (0.47 ml, 0.69 g, 7.0 mmol) and the ketone (11.3 mmol) were added to a solution of $CuCl_2$ (7.7 g, 58.0 mmol) in 30 mL dioxane (40% in water). The mixture was stirred at room temperature for 48 hrs. The progress of the reaction was monitored by TLC using hexane-ethyl acetate (85:15) as an eluting solvent.

The reaction was interrupted when 50% of the starting material was consumed and diluted with ether. The produced mixture was stirred at room temperature. The ether layer was separated, washed two times with 30ml of aqueous sodium bicarbonate (5%), then dried over Na_2SO_4 and concentrated in vacuo. The complex was separated from the residue by washing with toluene (2 x20 mL) dried and reused, the activity of the catalyst was evaluated.

2.6.1 α-Hydroxylation of Cyclohexanone from Cyclohexanone, Using polymeric polyimine–Pd complex

Cyclohexanone (1.2 mL, 11.3 mmol) was used to give 2-hydroxy cyclohexanone which was purified by distillation to give 1.3 ml of a yellow

liquid which boils at 186^{o}C. IR spectrum showed sharp stretching bands at 3400 cm^{-1} for O-H, at 1700cm^{-1} for C=O and at 1257cm,$^{-1}$ for C-O . NMR spectrum of the product showed the presence of a mixture of two Compounds, the starting material and α-hydroxy cyclohexanone (δ 3.48, s, OMe; and 4.25 dd, H on C2). According to ^{1}H-NMR results, the conversion of cyclohexanone to 2-hydoxycyclohexanone **15** was about 50 %, and that could be concluded from the peak integration. By comparing the integration of the peak at δ 4.33, (dd, C2-H) corresponds to one hydrogen with that at δ 2.1 (4H, t) correspond to four hydrogens (C-2 and C-6 H's in cyclohexanone). The catalyst were collected and dried and washed with toluene and kept for future use

2.6.2 α-Methoxylation of cyclohexanone Using polymeric polyimine – Pd complex

Cyclohexanone (1.32 mL,11.3mmol) in 20ml of methyl alcoholwas used to give 2-methoxycyclohexanone which was purified by distillation to give a yellow liquid (0.8 ml) . Its IR spectrum showed peaks at1712.7 cm^{-1} C=O, 2835 cm^{-1} OCH_3, and 1168 cm^{-1} C-O-C ether. The following NMR data indicating the formation of 2-meyhoxy cyclohexanone, and also shows the presence of a mixture of two compounds, the starting material and 2-methoxyl cyclohexanone **20** (δ 3.48, s, OMe; and 4.25 dd, H on C2). According to ^{1}H-NMR results, the conversion of cyclohexanone to 2-methoxycyclohexanone was about 50 %, and that could be concluded from the peak integration. By comparing the integration of the peak at δ 3.48,

(OMe, s) corresponds to three methoxy hydrogens with that at δ 2.1 (4H, t) correspond to four hydrogens (protons on C-2 and C-6 in cyclohexanone).

Also GC analysis indicated that we have a product depending on the peak resolution, the catalyst were collected and dried and washed with toluene.

2.6.3 α-Hydroxylation of Acetophenone Using polymeric polyimine –Pd complex

Acetophenone (1.3577 g , 0.0113 mol) was used to give 2-hydroxyacetphenone, which was purified by column chromatography on silica gel to give about 1.04 g (yield 56%) GC, IR cm^{-1}: 1690cm^{-1} for C=O, 3420 cm^{-1} for O-H and 1190 $cm^{-1}$for C-O alcohol gave an indication of the formation of the α-hydroxy acetophenone **16** as a mixture with the starting material (acetophenone). Also GC peak resolution gave two compounds of two different boiling points.

CHAPTER THREE
RESULTS AND DISCUSSION

It is intended from this work to device a convenient method for the synthesis of hydroxylated ketones and methoxy ketones at α-position (α-hydroxy ketones and α-methoxy ketones). α-Hydroxy and α-methoxy ketones are important intermediates for the synthesis of natural products, fine chemicals, and drugs.[57] For that reason, there is a considerable interest and there has been a number of reports on this topic.[58] One of the simplest approaches involves the reactions of enolates and enol derivatives[59]. Furthermore, α-Hydroxy ketones are useful building units in the preparation of biologically active compounds. The isomerization of α-Hydroxy ketones compounds is of crucial importance in metabolism process.

The importance of α-Hydroxy and α-methoxy ketones mentioned above brought us to investigate and describe the catalytic oxidation of ketones using two types of catalysts:

1. Pd(II) on polymeric polyimine supported catalyst
2. Pd (II) on natural product based polyimine ligands.

3.1 Synthesis And Investigation Of Catalytic Activities Of Pd(II) On Supported Polymeric Polyimine

Compounds containing one C=N functional group are called imines and those with two or more functional groups are called polyimins.

Polyimine was chosen for this study since it has high thermal stability, can be easily prepared, and forms relatively stable complexes with various transition metals such as palladium and platinum. Imines can be prepared by direct condensation of amines with carbonyl substrates such as aldehydes or ketones [60]. Simply, polymeric polyimine could be prepared in the same manner by condensation of alkyl polyamines with dialdehydes or diketones. Easy work- up of the reaction and purification of the product, combined with the availability of a wide spectrum of starting polyamines allow us to study the effect of various factors that influence catalytic activities of polymeric polyimine supported catalyst such as steric and electronic features.

The polyimine catalytic systems used in the present study as shown in scheme 3.2 consist of transition metal Pd (II) attached to polyimine, which affords multi-catalytic sites on the same polymeric chain.

The preparation of the polymeric polyimine catalytic support was carried out by treating polyimine with Pd (II) tetracetonitrile teteraflourborate $[Pd(CH_3CN)_4](BF_4)_2$ in polar aprotic solvent such as acetonitrile, followed by various thermal treatments.

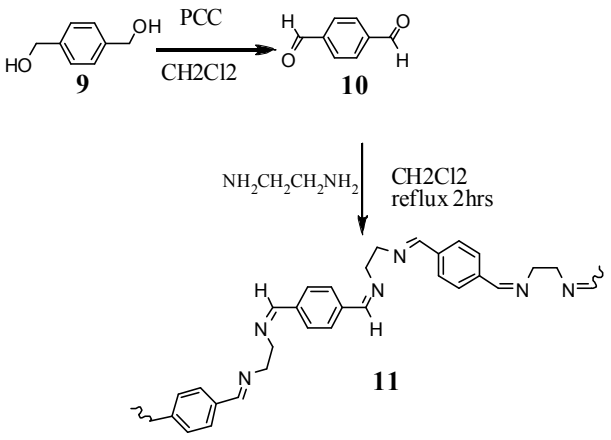
3.1.1 Synthesis of polymeric polyimine (11)

Polymeric polyimine was prepared in three steps as shown in Scheme 3.1. In the first step 1,4-benzenedimethanol **(9)** was oxidized using pyridinium chlorochromate (PCC) to 1,4-benzenedicarboxyaldehyde

(Terphathaldicarboxaldehyde) (**10**) in 80% yield. Compound **10** was analyzed by ^{1}H NMR and IR spectroscopy. IR spectra showed the presences of new bands which correspond to aldehyde (1695cm^{-1}, 2770 and 2855cm^{-1}) and the absence of the hydroxyl group of the starting material. Also the melting point of the dialdehyde (112-114C°) was consistent with the literature value (114 C°).[56]

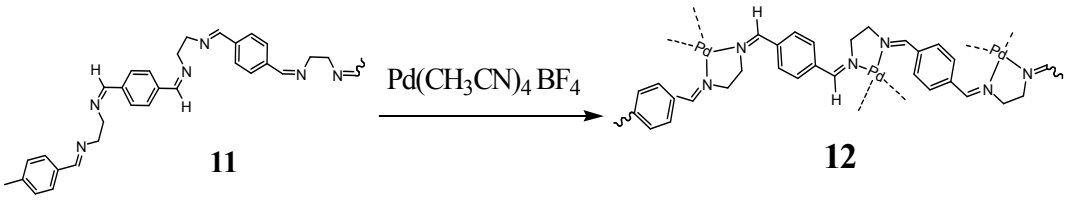
In the second step 1, 4-benzenedicarboxyaldehyde (**10)** was reacted with ethylenediamine in dichloromethane in the presence of molecular sieves or magnesium sulfate. Both reagents are known to bind with water, which is produced as a by product during this reaction. An outline of the synthetic pathway is shown in scheme 3.1. The IR spectrum of Polymer **11** showed no peaks for aldehyde but showed peaks at 1630 cm^{-1} and 3450cm^{-1} which indicates the complete conversion of **10** to **11.** Also, the solubility behavior and the high melting point (350 ºC) of the product indicate the formation of polymeric species.

Scheme 3.1



The lone pair of electrons on nitrogen makes the amine an ideal ligand for bonding to transition metals such as Pd (II). That brings the third step which is the preparation of Pd (II) polymeric polyimine **(12).** Polymeric polyimine **(11)** was treated with the catalyst Pd (II) tetracetonitrile teteraflourborate $[Pd(II)(CH_3CN)_4\ ](BF_4)_2$, prepared by the reaction of nitrosotetrafluroborate salt and palladium Sponge in freshly distillated acetonitrile in acetonitrile to give **(12)**. The immobilization of palladium (II)on polymeric polyimine shown in scheme 3.2

Scheme 3.2



The complexed-compound (12) was verified by the IR and NMR spectra. IR showed C=N stretching at 1630 cm^{-1}. Regular free polyimine usually shows C=N stretching band at 1680 cm^{-1}. According to this results the stretching frequency for C=N in complexed polyimine made a red shift by about 50cm^{-1}. This shift is due to the decreasing in the bond order of C=N. These results are in good agreement with the C=N and Pd (II) formation. [60]

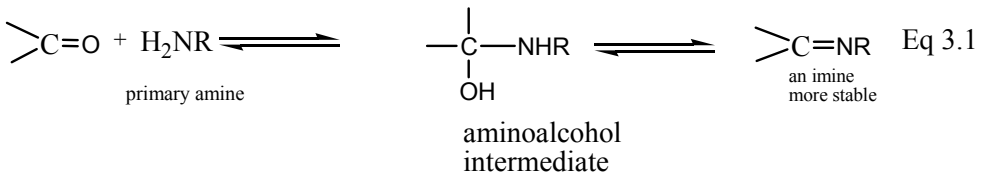
3.1.2 Synthesis of 1,4-Benzenedicarboxaldehyde (Terphthal dicarboxalaldehyde) (10) from oxidation of 1,4-Benzenedimethanol

Terphthal dicarboxalaldehyde **10** was produced from the oxidation of 1,4 –Benzenedimethanol (**9)** using pyridinium chlorochromate (PCC), a

mild oxidizing agent that converts alcohol into aldehyde but not into carboxylic acid. So the two hydroxyl groups of 1,4-benzenedimethanol were converted into dialdehydes using PCC. The dialdehyde oxidation produced was confirmed by IR spectrum. The appearance of C=O stretching band at 1695cm^{-1} and the aldehydic C-H stretching band at 2750 and 2850 cm^{-1} indicates the formation of aldehyde. Also the disappearance of the OH stretching band at 3400 cm^{-1} confirms the completion of the reaction. These results are good evidence for the transformation of the alcohol into aldehyde. (Fig.A1, Appendix A).[61, 62]

3.1.3 Synthesis of Polyimine (11) from Terphathaldicarboxaldehyde (10) in the presence of $MgSO_4$

As expected, amines react with carbonyl compounds by nucleophilic condensation reactions. Similar to other condensation reactions imine formation reaction is a reversible reaction, imines hydrolyze back to the amine and the carbonyl compound. Anhydrous magnesium sulfate ($MgSO_4$) was used to shift the equilibrium in favor of the formation of imine hence it absorbs water as it is formed. A general reaction of an amine and a carbonyl compound is shown in Equation 3.1, and since ethyelendiamine is a primary amine its addition to aldehyde is easily undergoes dehydration to form the imine carbon-nitrogen double bond.



Eq 3.1

The enamine tuatomer is not expected in this reaction of ours due to the lack of α-hydrogen on the carbonyl compound and the extra stability of the produced imine which has a C=N conjugation with the aromatic ring.

On the other hand, in the absence of anhydrous $MgSO_4$ equilibrium is reached and hence as product form it converts back to the starting material (amine and dialdehyde).

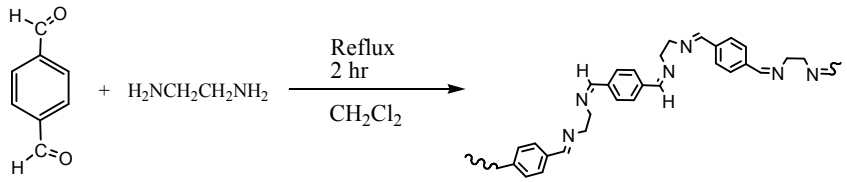
Comparison of the IR spectra (Fig A2, Appendix A) of the polyimine with that of the aldehyde (Fig A1,Appendix A) shows, that the sharp band at 1695cm^{-1} for the C=O stretching of the aldehyde disappeared and a new one appeared at 1643 cm^{-1} which indicates the formation of C=N bond. ^1H NMR showed signals that are consistent with the polymer structure: 7.82 (m, 2H, aromatic), 7.4 (m, 1H, aromatic), 7.3 (m, 1H, HC=N), 3.55 (s, 4H, CH_2CH_2), 2.48 (s, 6H, CH_3CN).

3.1.4 Synthesis of polyimine from Terphathaldicarboxaldehyde without $MgSO_4$

Synthesis of polyimine in the absence of $MgSO_4$ was carried out as shown in scheme 3.3. IR spectra indicate that the reaction was incomplete where some of the starting material was still present and that proves that the reaction reaches equilibrium. As shown in the IR spectrum (Fig.A3 Appendix A). The two bands at 1695 and 1643 cm^{-1} are for both C=O and C=N stretching respectively. The incomplete reaction could be attributed to the presence of free water that hydolyzed the imine back to starting

material (Scheme 3.3). This result was concluded by comparing of IR spectra of produced imines from both reactions with and without $MagSO_4$.

Scheme 3.3



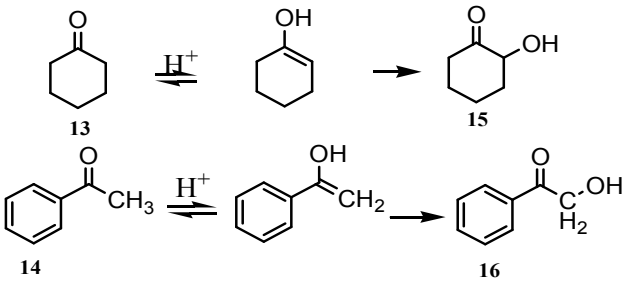
10
Terphthaldicarboxaldehyde

11
Polyimine

3.1.5 Hydroxylation of Cyclic ketones using the polymer supported catalysts

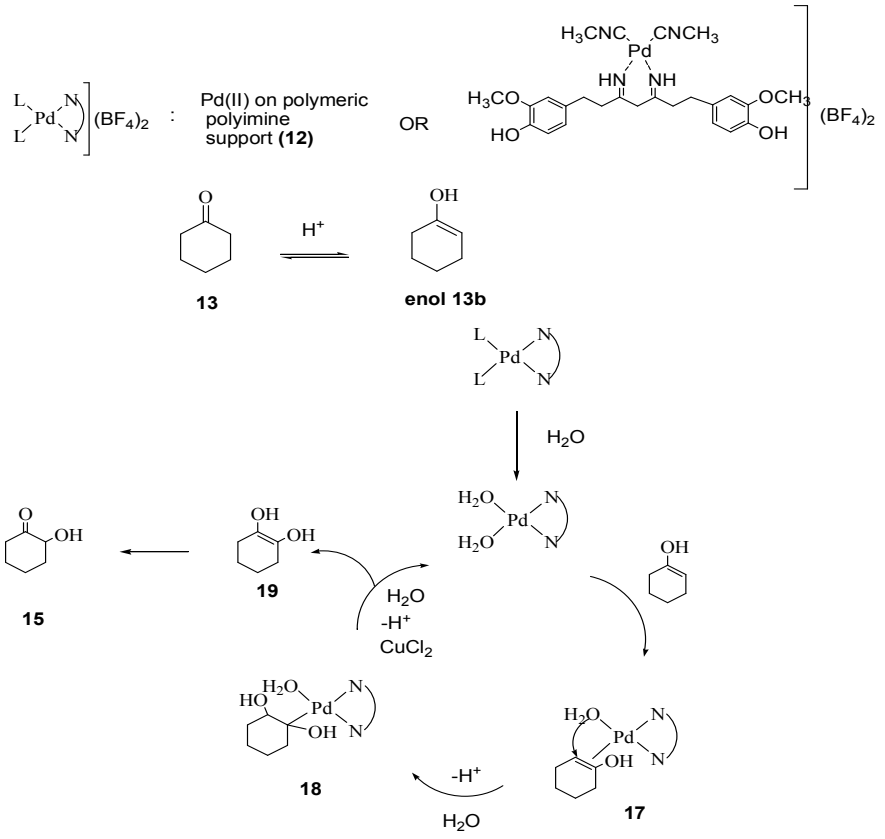
Hydroxylation of cyclic ketones (hydroxypalladation) is considered together with oxidation reaction of carbonyl. The oxidation of carbonyl by metals is well known and widely studied reactions. Many of these apparently reactions proceed through the oxidation of the enol tautomer. Hydroxypalladation of ketones was carried out in water in the presence of catalytic amount of Pd(II) on polymeric polyamine supported catalyst, re-oxidant, and small quantity of acid such as triflouroactic acid. The α-hydroxyketone product was characterized by ^{1}H-, ^{13}C-NMR, and FTIR spectroscopic methods. The α-Hydroxyketone namely 2-hydroxycyclohexanone (**15**) and 2-hydroxyacetophenone (**16**) were prepared in moderate yield from cyclohexanone (**13**) and acetophenone (**14**) respectively. The route of the formation of 2-hydroxycyclohexanone and 2-hydroxyacetophenone are shown in scheme 3.4.As expected hydroxylation was formed from enol which undergoes oxidation to the final product.

Scheme 3.4



The formation of product could be explained through the mechanism shown in scheme 3.5. As shown in the scheme, ketone in the presence of triflouroactic acid or methane sulfonic acid undergoes tautomerization to form the enol, which forms with Pd(II) the initial π-complex **17.** The π-complex **17** reacts with water by syn addition reaction to give the σ-complex **18**. Then **18** undergo β-elimination to give compound **19** which undergoes tautomerization to give the final product α-hydroxyketone **15**.

Scheme 3.5



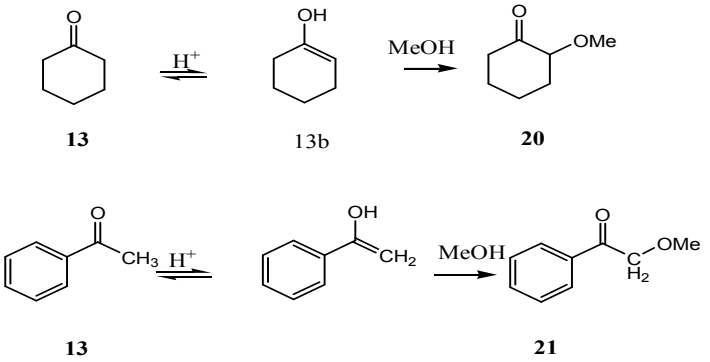
Cupric chloride was used as a re-oxidant for Pd (0) in which it converts Pd(0) back to the active catalytic spices Pd(II). As mentioned earlier the products were characterized by ^{1}H NMR and FTIR. ^{1}H NMR spectrum for 2-hydroxycylohexanone (**15**) showed NMR signals that are consistent with the structure (see the experimental part).

3.1.6 Methoxylation Of Cyclic Ketones Using The Polymer Supported Catalysts

Methoxylation of cyclic ketones is also considered like hydroxypalladation oxidation reaction of carbonyl**.** Methoxyaltion of carbonyl proceeds through oxidation of the enol tautomer as shown in scheme 3.7.

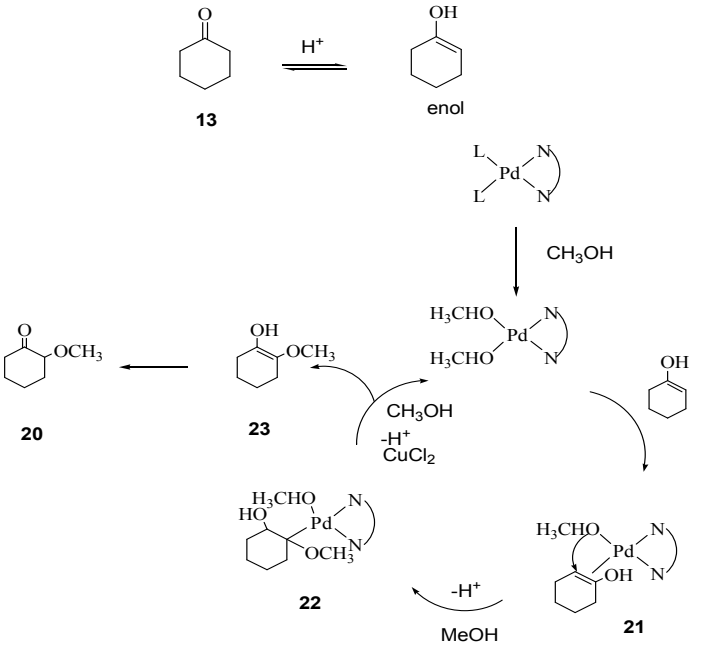
Methoxylation of ketones was carried out in methaol in the presence of catalytic amount of Pd(II) on polymeric polyamine supported catalyst, re- oxidant, and small quantity of triflouroactic acid. The characterization of the α-methoxyketone product was achieved by using spectroscopic techniques such as ^{1}H-, ^{13}C-NMR, and FTIR. The α-Methoxyketone namely 2-methoxycyclohexanone (**20**) was prepared from cyclohexanone (**13**) in moderate yield. The route of the formation of 2-methoxycyclohexanone is shown in scheme 3.6 below. As you can see, the first step in both schemes 3.4 and 3.6 are similar.

Scheme 3.6



The product formation could be explained in a similar fashion to that of the hydroxypalladation shown in scheme 3.5. As shown in the scheme, ketone in the presence of an acid undergoes tautomerization to form enol, which froms with Pd(II) the initial π-complex **21.** The π-complex **21** reacts with methanol by syn addition reaction to produce the σ-complex **22**. Then compound **22** undergoes β-elimination to give compound **23** which undergoes tautomerization to give the final product α-methoxycyclohexanone **20**.

Scheme 3.7



Cupric chloride was used as a re-oxidant for Pd (0), in which it converts Pd (0) back to the active catalytic spices Pd(II). The Pd (II) on polymeric polyimine catalyst was recycled several times, and showed a good activity upon reuse. At the end of each catalytic cycle the catalyst was washed by toluene, and reused to catalyze same kind of reaction. As mentioned earlier the exact percentage recovery of the catalyst could not be calculated for the time being due to technical difficulties. This way it has been proved that this catalyst is environment-friendly since small amounts of it needed hence it could be used over and over. However, it has been noticed that the reactivity of the reused catalyst decreased with the number of its using times. This decrement could be attributed to dislodging of the Pd (0) precipitate from the polymer support before it has been re-oxidized back to Pd (II). The activity of the Cu (II) re-oxidant could be enhanced by introducing oxygen to the reaction mixture, this way the precipitation of Pd (0) could be minimized.

3.2 Synthesis and Investigation of Catalytic Activities of Pd (II) on Imine Based-Curcumin ligands (26)

3.2.1 Extraction and purification of Curcumin (6)

The natural product curcumin was chosen because it contains 1,3-dicarbonyl groups which could be converted into an imine derivatives that can be complexed with palladium(II) to form the desired catalyst. Curcumin was extracted from turmeric and purified by flash chromatography as shown in the experimental part. NMR spectra for the

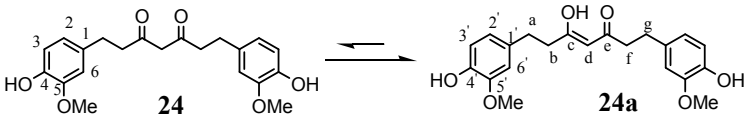
extracted curcumin were in agreement with the structure shown in Scheme 3.8.

^{1}H NMR ($CDCl_3$-DMSO, d6) 8:2: δ= 9.45 (broad, 1H, OH vinylic), 7.45-7.55 (m, 2H, aromatic), 7.25 (d, 1H, aromatic), 7.05 (dd, 2H), 6.85 (m, 2H, vinylic), 6.7 (d, 2H, vinylic), 5.9 (s, 1H, OH) 3.85 (s, 6H, OMe). ^{13}C NMR ($CDCl_3$-DMSO 8:2, d6): δ= 184 (C=O), 149, 148, 140.5, 130, 127, 124, 121, 115, 115.5, 112, 101, 56. The IR spectrum (Fig A8) showed the bands at 3502 cm^{-1}, for OH stretching, at 3386 cm^{-1} for the enol due of hydrogen bonding, and at 1620 cm^{-1} for C=C and these values lowered.

3.2.2 Preparation of Tetrahydrocurcuminoid (THC) (24)

Curcumin was converted into imine derivative in two steps as shown in scheme 3.8. The first step involves hydrogenation of curcumin using Pd/C catalyst under a pressure of 5 psi of H_2 to produce tetrahydrocurcuminoid (THC). THC was analyzed by ^{1}H- and ^{13}C-NMR. NMR spectra showed signals that are consistent with the structure. ^{1}H NMR showed the following signals: δ= 6.8 (d, J = 8.24, 2H, aromatic), 6.62 (d, J = 8.42 =2H, aromatic), 6.6 (s, 2H), 5.6 (br, 2H, OH), 5.4 (s, 0.75 H, vinylic), 3.90 (s, 0.5H, diketone), 3.85 (s, 6H, OCH_3), 2.9 (t, J = 7.97, 3H), 2.6 (t, J = 7.14, 3H). ^{13}C NMR ($CDCl_3$) showed the following signals: δ= 193.2 (Cc and Ce), 144.5 (C4'), 143.9 (C3'), 132.5 (C1'), 120.7 (C6'), 114.3 (C2'), 110.9 (C5'), 99.8 (Cd), 55.8 (OMe), 40.4 (Cb, Cf), 31.1 (Ca, Cg). The second step is explained in the next section.

Scheme 3.8



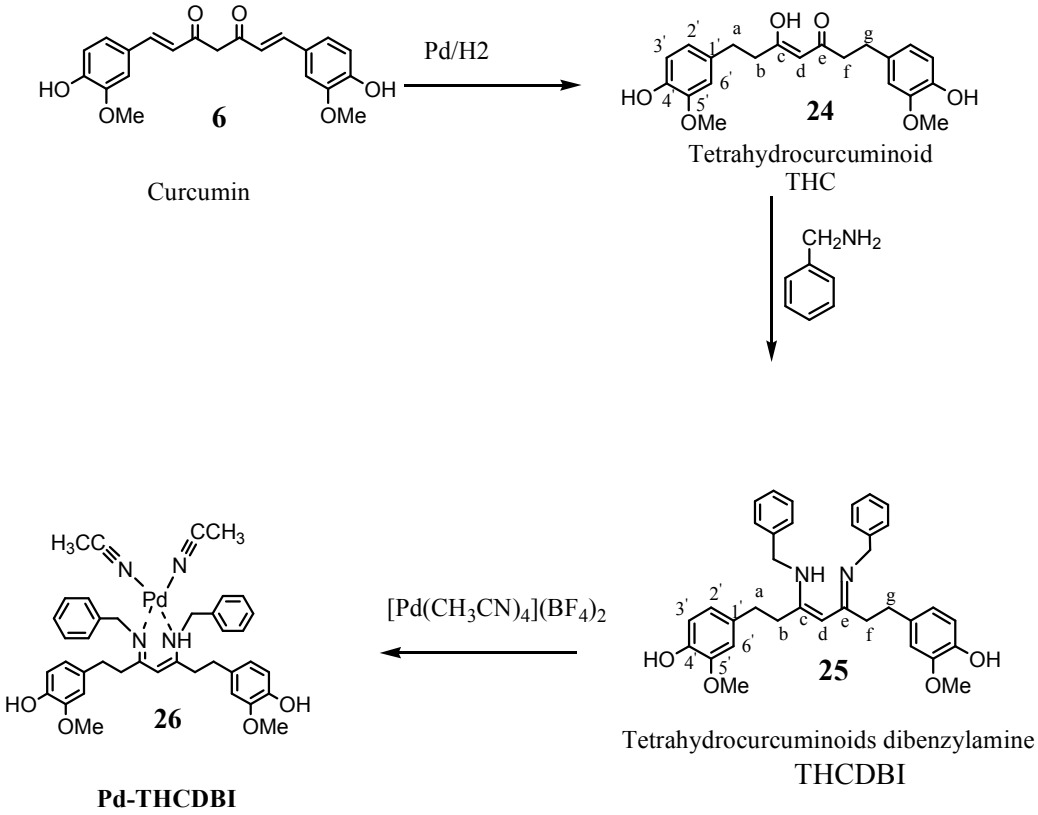
Tetrahydrocurcuminoids

THC

3.2.3 Converting Tetrahydrocurcuminoid (24) Into Tetrahydrocurcumin Dibenzylimine (25)

Tetrahydrocurcumenoid was then converted into imine by similar procedure used for the preparation of the polymeric polyimine. THC **(24)** was reacted with two equivalents of benzylamine to afford tetranhydrocorcumenoid dibenzylamine (THCDBI, **25)**. An attempt to convert curcumin **24** to its corresponding imine was unsuccessful and that could be attributed to the conjugation with an alkene which reduces the elctrophilicity of carbonyl carbon. The THCDBI **25** was also analyzed by ^{1}H- and ^{13}C -NMR. ^{1}H NMR (300 MHz) ($CDCl_3$): δ= 11.3 (br, 0.37H, NH enamine), 9.9 (br, 2H, OH), 7.2-7.45 (m, 16H, arom), 5.6 (br, 2H, NH), 5.3 (s, 0.75 H, vinylic), 4. 12 (s, 4H, $PhCH_2$), 3.85 (s, 6H, OCH_3), 2.9 (t, J = 7.97, 4H), 2.6 (t, J = 7.14, 4H). ^{13}C NMR ($CDCl_3$ d6): δ= 165.2 (Ce), 158 (Cc), 133 (C1), 122.5 (C2), 115.5 (C3), 144.5 (C4), 147 (C5), 113 (C6), 98.8 (Cd), 56.8 (OMe), 34.5 and 35.6 (Cb, Cf), 30.1 (Ca, Cg).

Scheme 3.9



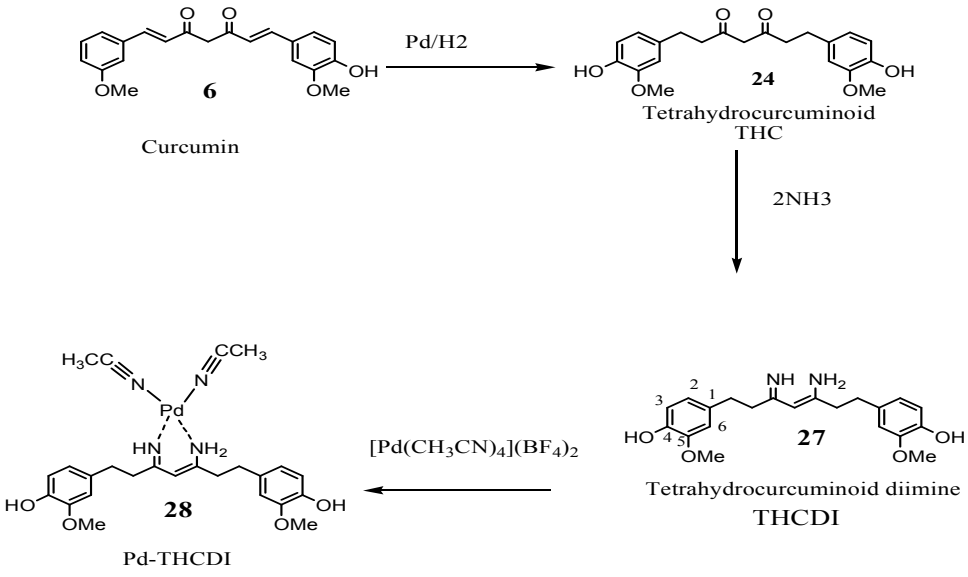
3.2.4 Synthesis of Pd-THCDBI Complex (26)

In the last step THCDBI **(25)** was reacted with Pd (II) tetrakis acetonitrile bis teteraflourborate $[Pd(CH_3CN)_4](BF_4)_2$ (THCDI) to afford a yellow golden solid complex (**26**). Elemental analysis showed that complex **(26)** contains Pd (10.2%, theoretical value = 14.5%) which suggests incomplete reaction. ^{1}H-NMR of the produced complex showed broad signal which could be attributed to the complexation with Pd(II). Signal multiplicity is not clear; however chemical shifts are consistent with the anticipated structure.

3.3 Synthesis and characterization of Palladium (II)-THCDI Complex (28)

Tetrahydrocucuminoiddiimine Palladium (**28**) was prepared in three steps as shown in scheme 3.10 in a similar fashion to the preparation of Pd(II)-THCDBI (**26**) complex. In this case THC (**24**) was treated with ammonia instead of benzylamine to afford tetrahydrocurcumin-dimine ligand (THCDI) (**27**). THCDI was then reacted with tetrakis acetonitrile palladium (II) tetrafluoroborate to produce Pd(II)-THCDI. As for others the prepared ligand THCDI (**27**) and the Pd(II) of THCDI were analyzed by ^{1}H-NMR and ^{13}C-NMR. ^{1}HNMR ($CDCl_3$)**:**δ= 5.8 (m, 2H), 6.7 (s, 1H, vinylic H), 6.6 (m, 4H, arom), 5.5 (2H, NH_2), 3.85 (s, 6H, OCH_3), 2.5- 2.9 (m, 8H) ppm. ^{13}C NMR ($CDCl_3$ d6) :δ= 164.2 (Ce), 147.3 (Cc), , 144.1 (C4'), 115.5 (C3'), 133.7 (C1'), 114.3 (C6'), 129.5 (C2'), 146.5 (C5'),55.7 (Cd), 49.6 (OMe), 40.1 (Cb, Cf), 29.7 (Ca, Cg) ppm. Elemental analysis showed that the complex **28** contains Pd (12.3%, theoretical value = 14.5%).

Scheme 3.10



3.4. Pd (II)-Curcumin based Imine Ligands Catalyzes hydroxypalladation and Methoxypalladation of Ketones

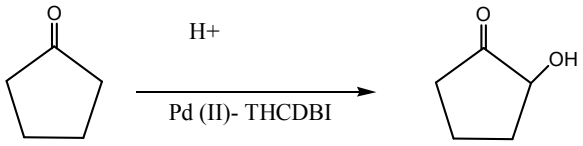
Pd(II) THCDBI (**26**) and THCDI (**28**) were used to catalyze the hydroxylation and methoxylation of ketones in the same way as for Pd(II) polymeric polyimine support (**12**) that motioned before. The results are summarized in Table 3.1. Also table 3.1 also contains results obtained from Pd(II) polymeric polyimine support. As can be seen in table 3.1, the percentage yields were low. Some starting materials were observed by GC-MS, which means that the conversion was incomplete. This low yield could be related to more than one reason: (1) stability of imine ligand in a aqueous solution is limited due to reversible reaction mentioned earlier; (2) full catalytic activities wasn't reached, and that could be related to reaction conditions; hence various reaction conditions ought to be examined to determine which give best results. The reaction mechanism for the formation of methoxyketones and hydroxyketones is expected to be similar to that shown in Schemes 3.5 and 3.7.

Table 3.1

Starting Material	Catalyst	Product	% Yield
Cyclohexanone	Pd(II)THCDBI	α-Hydroxy cyclohexanone	47%
Cyclopentanone	Pd(II)THCDBI	α-HydroxyCyclopentanone	72%
Acetophenone	Pd(II) polymeric Polyimine	α-Hydroxy acetophenone	54%
Cyclohexanone	Pd(II) polymeric Polyimine	Methoxy cyclohexanone	52%
Propiophenone	Pd(II)THCDBI	α-Hydroxy Propionone	41%
Propiophenone	Pd(II)THCDI	α-Hydroxy Propionone	32%
2-Methyl cyclohexanone	Pd(II)THCDBI	6-Methyl-2-hydroxycyclohexanone	49%
Cyclohexanone	Pd(II)THCDI	α-Hydroxy Cyclohexanone	37.5%
Cyclohexanone	Pd(II) polymeric Polyimine	α-Hydroxy Cyclohexanone	50%

3.4.1. α-Hydroxypalladation of Cyclopentanone (29) Using Pd (II)-THCDBI Complex (26)

Hydroxypalladation of cyclopentanone using complex (**26)** was carried out as before in water in the presence of re-oxidant $CuCl_2$ and small quantity of triflouroactic acid. Equation 3.2 summarizes the reaction. As shown in Table 3.1, the highest yield among all reactions was hydroxycyclopentanone (30). THCDBI (26) afforded 2-hydroxycyclopenatnone in about 72 % yield. The product was purified by column chromatography and characterized by ^{1}H-, and ^{13}C-NMR. 1H-NMR (300 MHz, $CDCl_3$): δ 1.66 (1H, s, OH), 1.88-2.38 (m, 6H), 4.10 (t, 1H, J=7.35 Hz) ppm. ^{13}C NMR (100 MHz, CDCl3) δ: 19.3, 33.5, 35.1, 58.3, 210.8.



Eq. 3.2

29
Cyclopentanone

30
2-Hydroxycyclopentanone

3.4.2 α-Hydroxypalladation of Cyclohexanone using Pd (II)-THCDBI Complex (26)

Hydroxypalladation of cyclohexanone using catalyst **(26)** or **(28)** was carried out as before in water in the presence of re-oxidant $CuCl_2$ and small quantity of triflouroactic acid. THCDBI **(26)** afforded 2-hydroxycyclohexanone in about 47 % yield, while THCDI afforded 2-hydroxycyclohexanone in about 37.5 % yield. Equations 3.3 and 3.4

summarize the reactions. The products were purified by column chromatography and characterized by ^{1}H-NMR and ^{13}C-NMR. ^{1}H NMR (300 MHz) ($CDCl_3$) δ: 1.41–1.65 (4H, m), 2.23 (1H, br, OH), 2.21–2.45 (4H, m), 4.13 (1H, q, J = 6.25 Hz, CH–OH); ^{13}C NMR (300 MHz) ($CDCl_3$): δ = 20.0, 22.8, 26.9, 32.9, 40.9, 75.9, 203.7. FTIR (neat): 3146, 2969, 1790, 1716, 1383, 1097 cm^{-1}

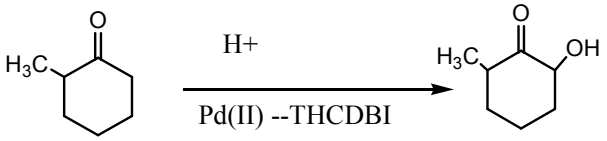
Cyclohexanone 2-Hydroxycyclohexanone **Eq. 3.3**

Cyclohexanone 2-Hydroxycyclohexanone **Eq.3.4**

3.4.3. α-Hydroxypalladation of 2-methylcyclohexanone Using Pd (II)-THCDBI (26) Complex

Hydroxypalladation of 2-methylcyclohexanone using complexes **(26)** and **(28)** was carried out as before in water in the presence of re-oxidant $CuCl_2$ and small quantity of triflouroactic acid. Equation 3.5 summarizes the reaction. As shown in Table 3.1, the major product was 2-hydroxy-6-methyl-cyclohexanone and its dehydration product. THCDBI **(26)** afforded 2-hydroxycy-6-methylclohexanone (**32**) in 49 % yield, while THCDI **(28)** afforded 2-hydroxy-6-methylcyclohexanone in 36.5 % yield. The product was purified by column chromatography and characterized by ^{1}H- and ^{13}C-NMR δ= 1.04 (d, 3H, J/6.8 Hz), 1.55 (1H, s, OH), 1.71-1.79

(m, 2H), 2.1 (m, 1H), 2.2 (m, 1H), 2.20-2.30 (m, 2H), 2.56 (dd, 1H, J-5.08, 8.65 Hz), 4.22 (t, 1H, J 7.38 Hz). ^{13}C-NMR (300 MHz, CDCl3): δ = 21.7, 28.1, 33.9, 34.3, 44.9, 60.4, 204.1 ppm. FTIR (neat): 3150, 2973, 1796, 1717, 1383, 1097cm^{-1}. ^{1}HNM (300 MHz, CDCl3) for 2-methyl cyclohex-2-en-1-one: δ: 1.86 (s, 3H), 1.97 (m, 2H), 2.43 (q, 2H, J 5.70 Hz), 2.52 (t, 1H, J7.0 Hz), 5.93 (t, 1H, J4.76 Hz). ^{3}C-NMR (300 MHz, CDCl3): δ= 23.0, 24.4, 38.9, 44.9, 116.3, 151.5, 194.4.



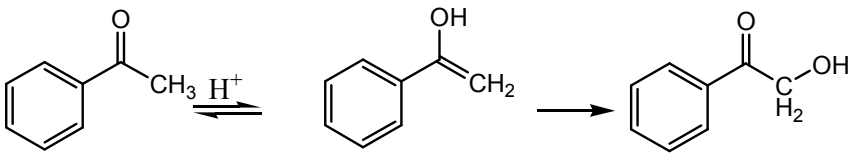
Eq3.5

2-Methylcyclohexanone

2-Hydroxy, 6-methylcyclohexanone

3.4.4 α-Hydroxypalladation of Acetophenone (16) Using Pd (II)-Polymeric polyimine complex (12)

Hydroxypalladation of acetophenone using catalyst **(12)** was carried out as before in water in the presence of re-oxidant $CuCl_2$ and small quantity of acid such as triflouroactic acid. Equation 3.6 summarizes the reaction. As shown in Table 3.1, the major product was 2-hydroxyacetophenone **(16)**. Pd (II)-Polymeric polyimine complex (**12**) afforded 2-hydroxyacetophenone (**16**) in 54% yield. The product was purified by column chromatography and characterized by ^{1}H-, ^{13}C-NMR, and FTIR. ^{1}H NMR (300 MHz) (CDCl3): δ= 7.78 (2H, m), 7.46 (2H, m), 7.6 (1H, m), 4.82 (1H, CH-OH, q), 3.6 (1H, s, OH), 1.52 (3H, d), ^{13}C NMR (300 MHz) ($CDCl_3$): δ = 198.2, 134.0, 132.7, 127.6, 126.5, 71.2, 21.8. FTIR (neat): 3420, 3060, 2959, 1730, 1690, 1383, 1190 cm^{-1}.

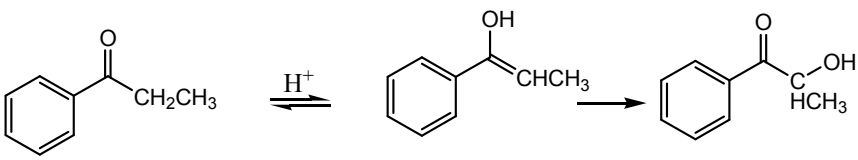


Eq 3.6

14 **16**

3.4.5 α- Hydroxypalladation of Propiophenone (35) using Pd(II)-THCDBI complex

Hydroxypalladation of propiophenone (**34**) using catalyst (**26)** or (**28)** was carried out as before in water in the presence of re-oxidant $CuCl_2$ and small quantity of triflouroactic acid. Equation 3.7 summarizes the reaction. As shown in Table 3.1, the major product was α-Hydroxypropiophenone (**35**). THCDBI (26) afforded α-Hydroxypropiophenone (**35**) in 41 % yield, while THCDI (28) afforded α-Hydroxypropiophenone (**35)** in 32 % yield. The products were purified by column chromatography and characterized by ^{1}H-, ^{13}C-NMR, and FTIR, as 2-hydroxypropiophenone **(35)**. ^{1}H NMR (300 MHz) (CDCl3): δ = 7.78 (2H, m), 7.46 (2H, m), 7.6 (1H, m), 4.82 (1H, CH-OH, q), 3.6 (1H, s, OH), 1.52 (3H, d), ^{13}C NMR (300 MHz) ($CDCl_3$): δ = 198.2, 134.0, 132.7, 127.6, 126.5, 71.2, 21.8. FTIR (neat): 3146, 3060, 2959, 1730, 1716, 1383, 1097 cm^{-1}



Eq 3.7

34 **35**

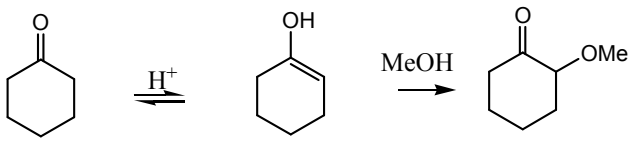
3.5 α-Methoxypalladation of Cyclohexanone using polymeric polyimine complex (12)

Methoxypalladation of cyclohexanone using complex **(12)** was carried out in methanol in the presence of re- oxidant $CuCl_2$ and small quantity of trichlorosulfonic acid. Equation 3.8 summarizes the reaction. As shown in Table 3.1, the major product was 2-methoxycyclohexanone.

Complex **(12)** afforded 2-methoxycyclohexanone (**20)** in 52% yield. The product was purified by column chromatography and characterized by ^{1}H-, ^{13}C-NMR, and FTIR. Its IR spectrum showed peaks at 1728.1 cm^{-1} C=O, 2835 cm^{-1} OCH_3, and 1168 cm^{-1} C-O-C ether. The following NMR data indicate the formation of 2-meyhoxycyclohexanone and show the presence of a mixture of two compounds: the starting material and 2-methoxyl cyclohexanone **(20)** (δ 3.48, s, OMe; and 4.25 dd, H on C2).

According to ^{1}H-NMR analysis using peak integration, conversion of cyclohexanone to 2-methoxycyclohexanone was achieved about 50 % yield.

By comparing the integration of the peak at δ 3.48, (OMe, s) corresponds to the three methoxy hydrogens with that at δ 2.1 (4H, t) correspond to four hydrogens (protons on C-2 and C-6 in cyclohexanone). Also GC analysis indicated that we have a product and this done by the peak resolution values.



Eq.3.8

13 **20**

Conclusion and Suggestions for Future work

Three new Pd (II) catalysts have been prepared and analyzed. Two of them namely Pd (II)-Tetrahydrocurcminoid dibenzylimine (**26**) and Pd (II)-Tetrahydrocorcumindiimine (**28**) are natural based complexes, which made from the renewable material curcumin. The third one is Pd (II) on polymeric polyimine support (**12**). The first two are homogenous catalysts while the third one is a heterogeneous one. The three catalysts were used to catalyze new reactions such as hydroxylation and methoxylation of ketones. The new synthetic methods could be valuable for natural product synthesis and medicinal chemists. Based on the results obtained from our work the polymeric catalysts are preferable since they are recyclable and hence can be used over and over for several times without loosing much of their activities. The novelty of the polymeric support developed here is that it has multicatlytic sites, which makes them one of the very few examples in the literature wherein a polymeric support with number of catalytic sites equal to the number of the repeat units.

In addition to the above accomplishment, the work reported in this thesis is a model and with this model we have shown that synthesis of α-substituted ketone could be a catalytic process. This process could be a base for novel method for asymmetric synthesis of α-substituted ketones.

This could be accomplished by replacing the imine ligands with chiral amine ligands; this way instead of preparing racemic α-substituted ketone, optically active α-substituted ketone could be prepared. α- substituted ketone will be used as a starting material for drugs and natural product synthesis.

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Appendices

Appendix A: FTIR Spectra for the compounds

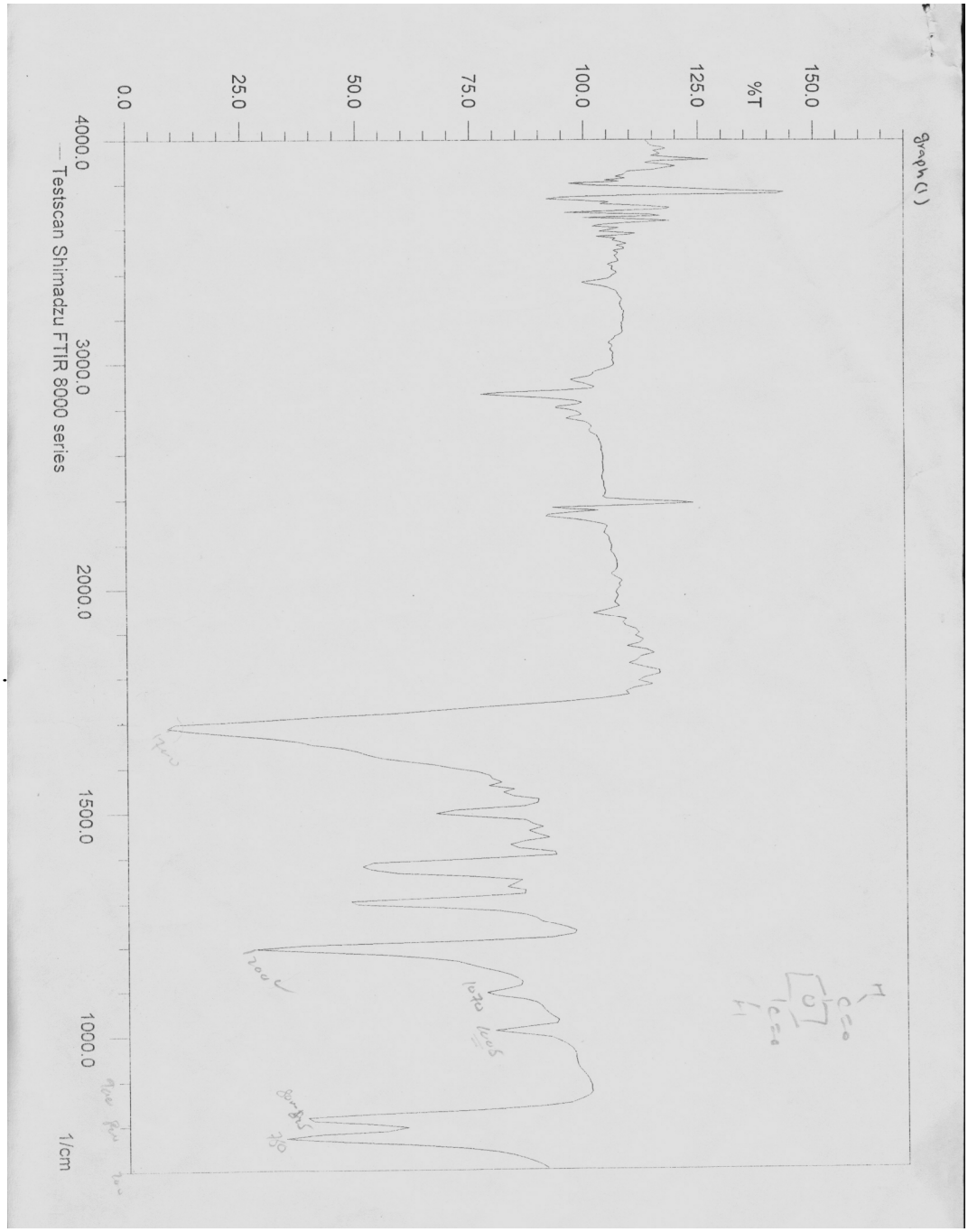


Fig A1: FTIR for 1, 4-Benzenedicarboxaldehyde (10) from oxidation of 1,4-Benzenedimethanole(9).

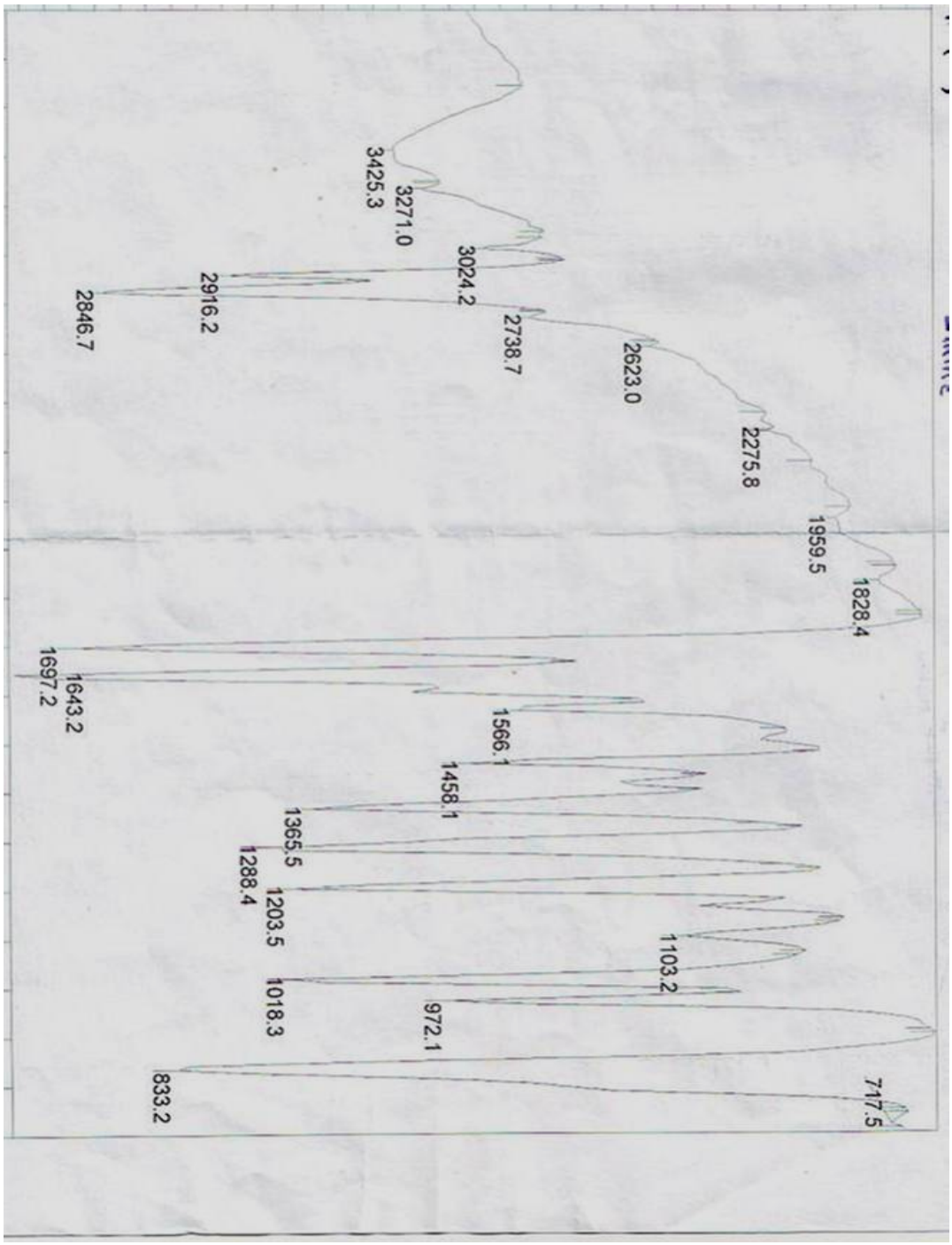


Fig A2: FTIR for Polyimine (11) from 1,4 Benzene dicarboxaldehyde Without $MgSO_4$.

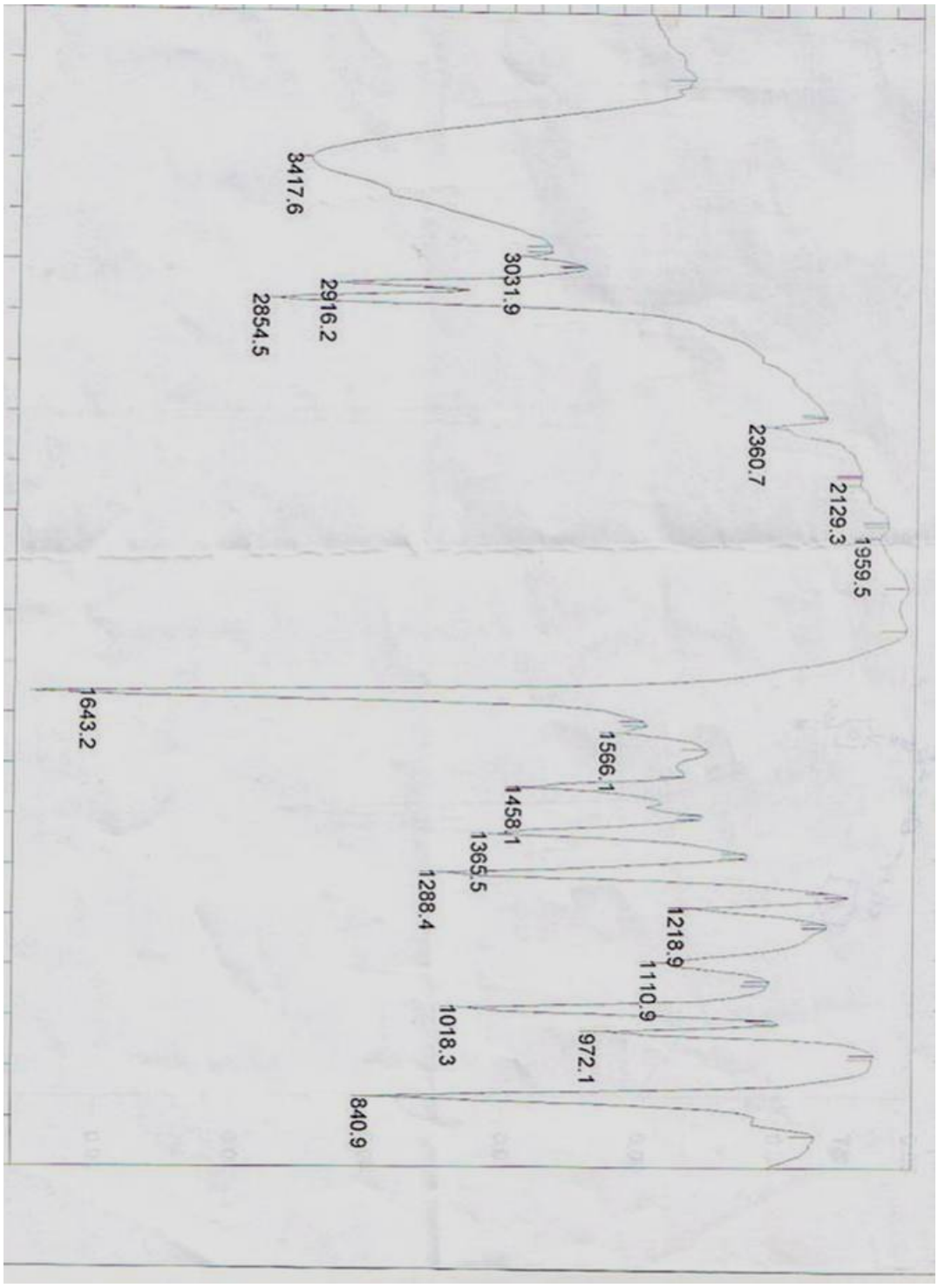


Fig A3: FTIR for Polyimine (11) from 1,4-Benzene dicarboxaldehyde in presence of $MgSO_4$

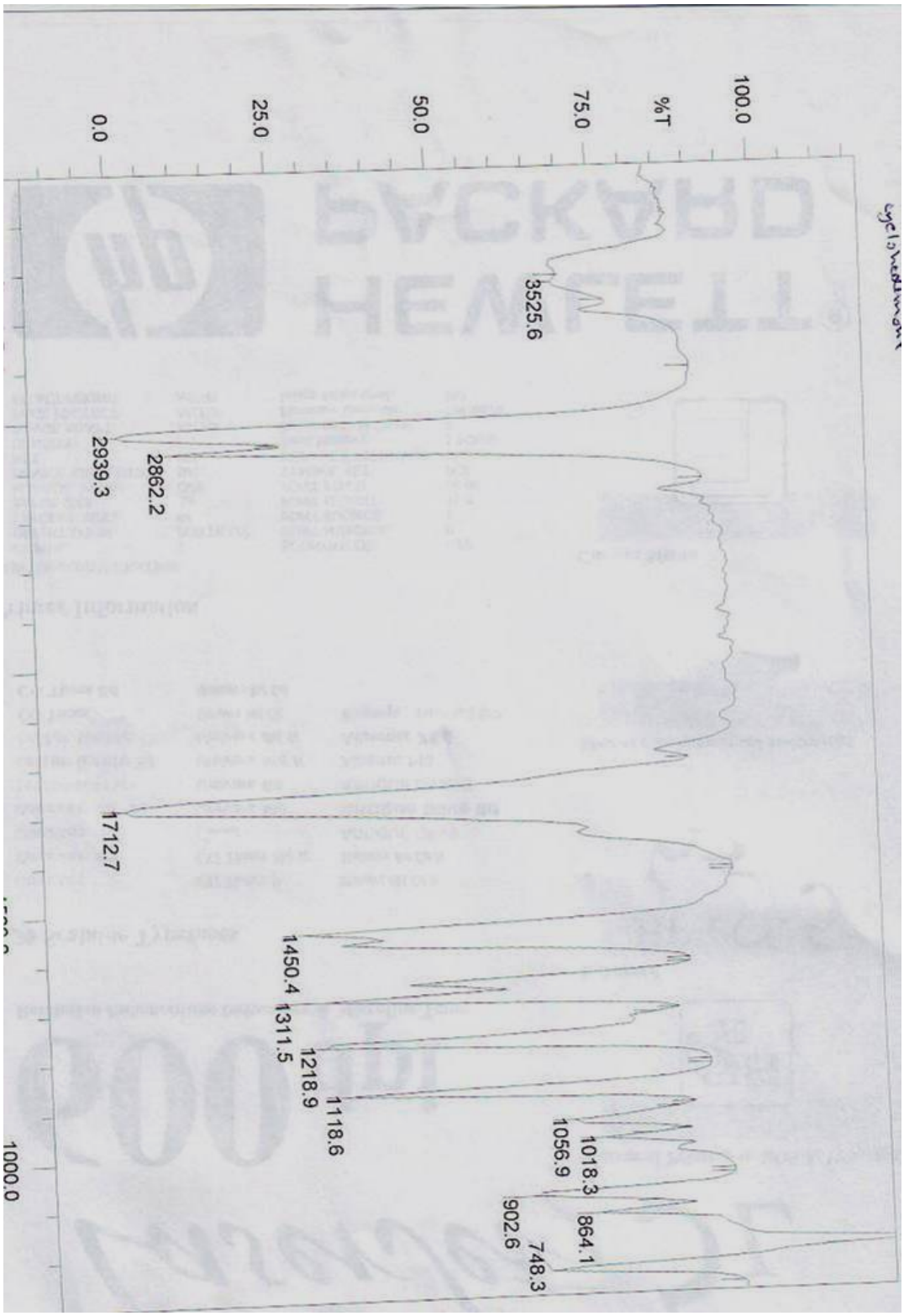


Fig A4: FTIR for Cyclohexanone (13) as starting material.

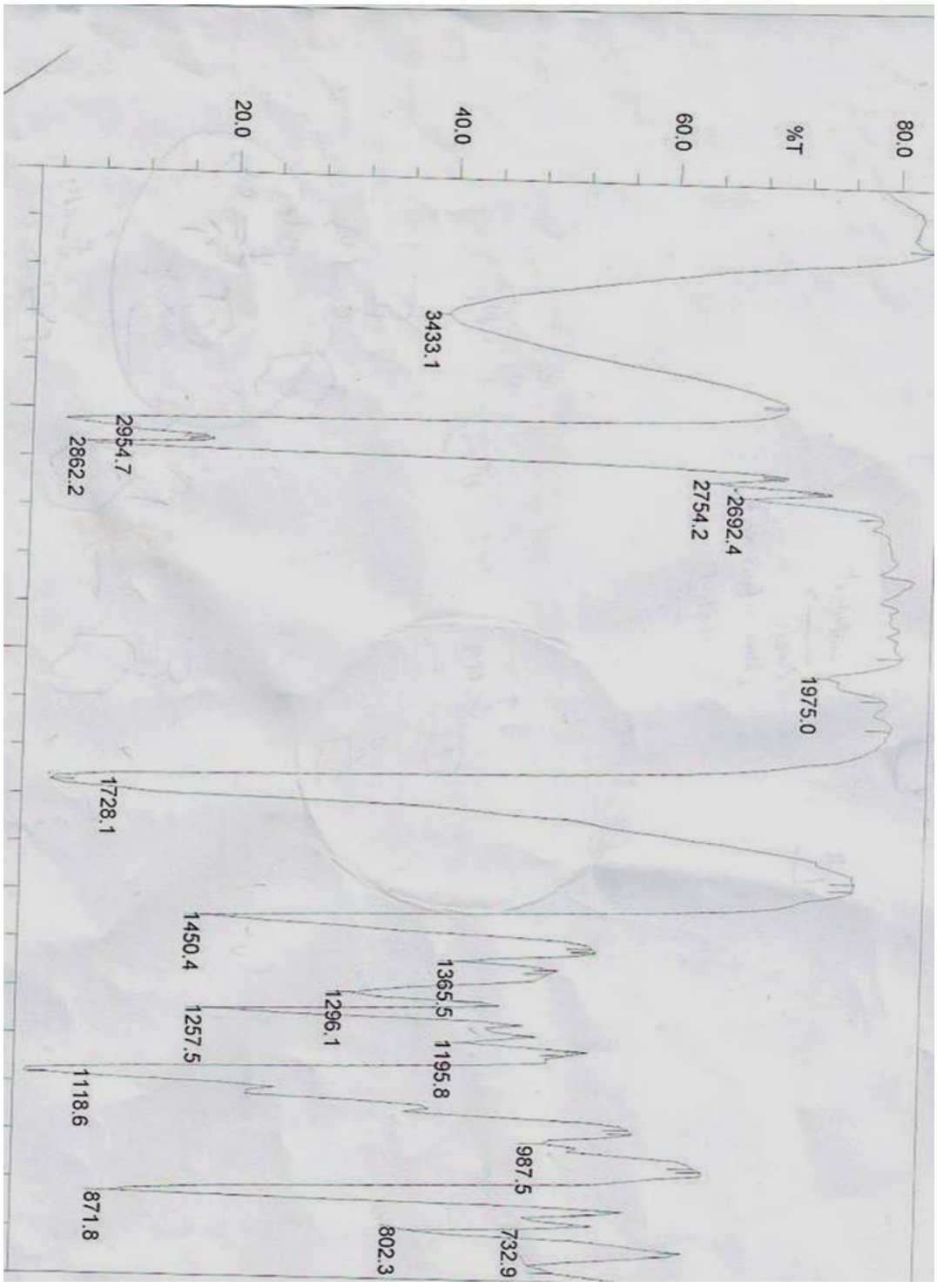


Fig A5: FTIR for α- Hydroxy Cyclohexanone (15) from Cyclohexanone hydroxylation.

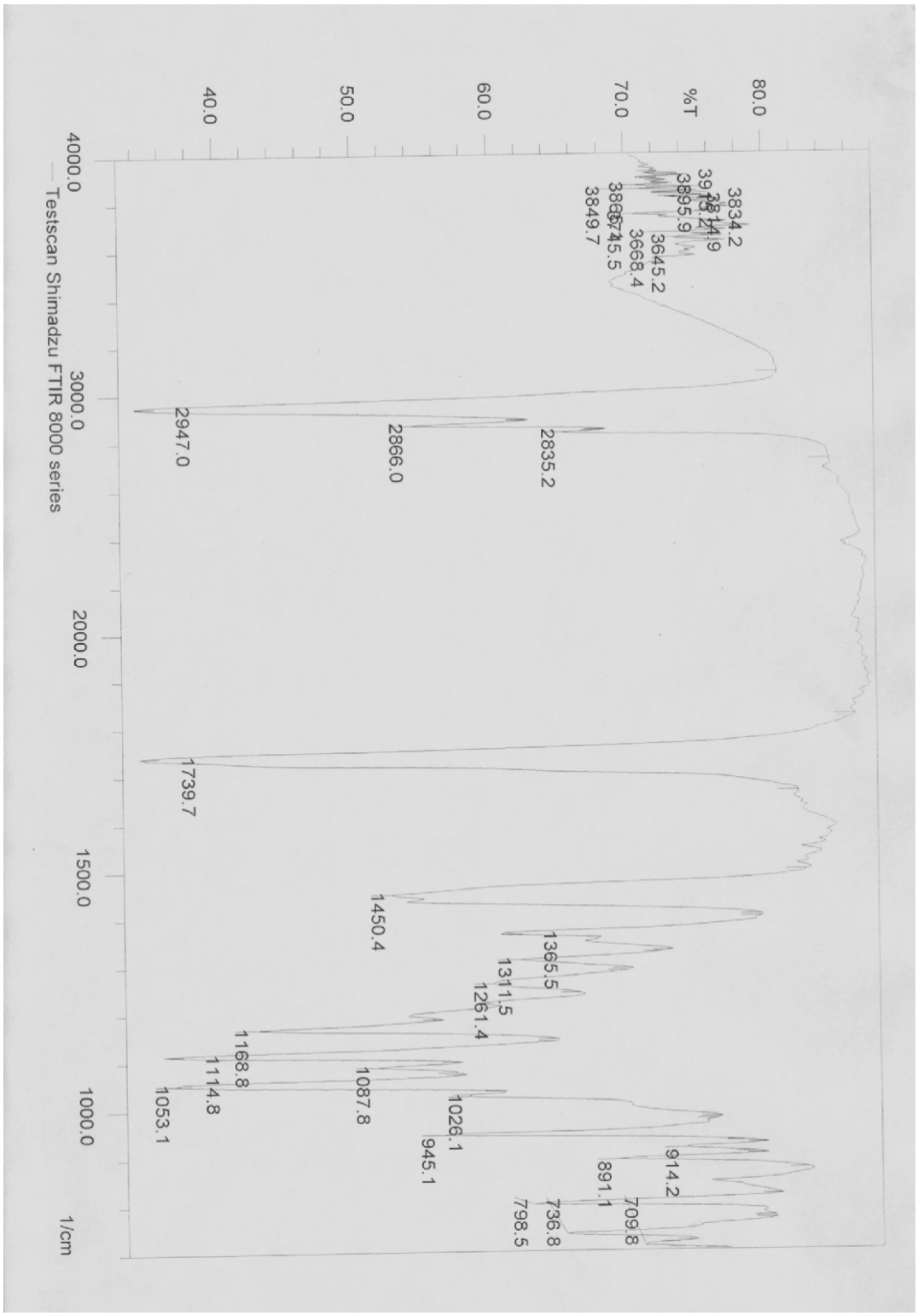
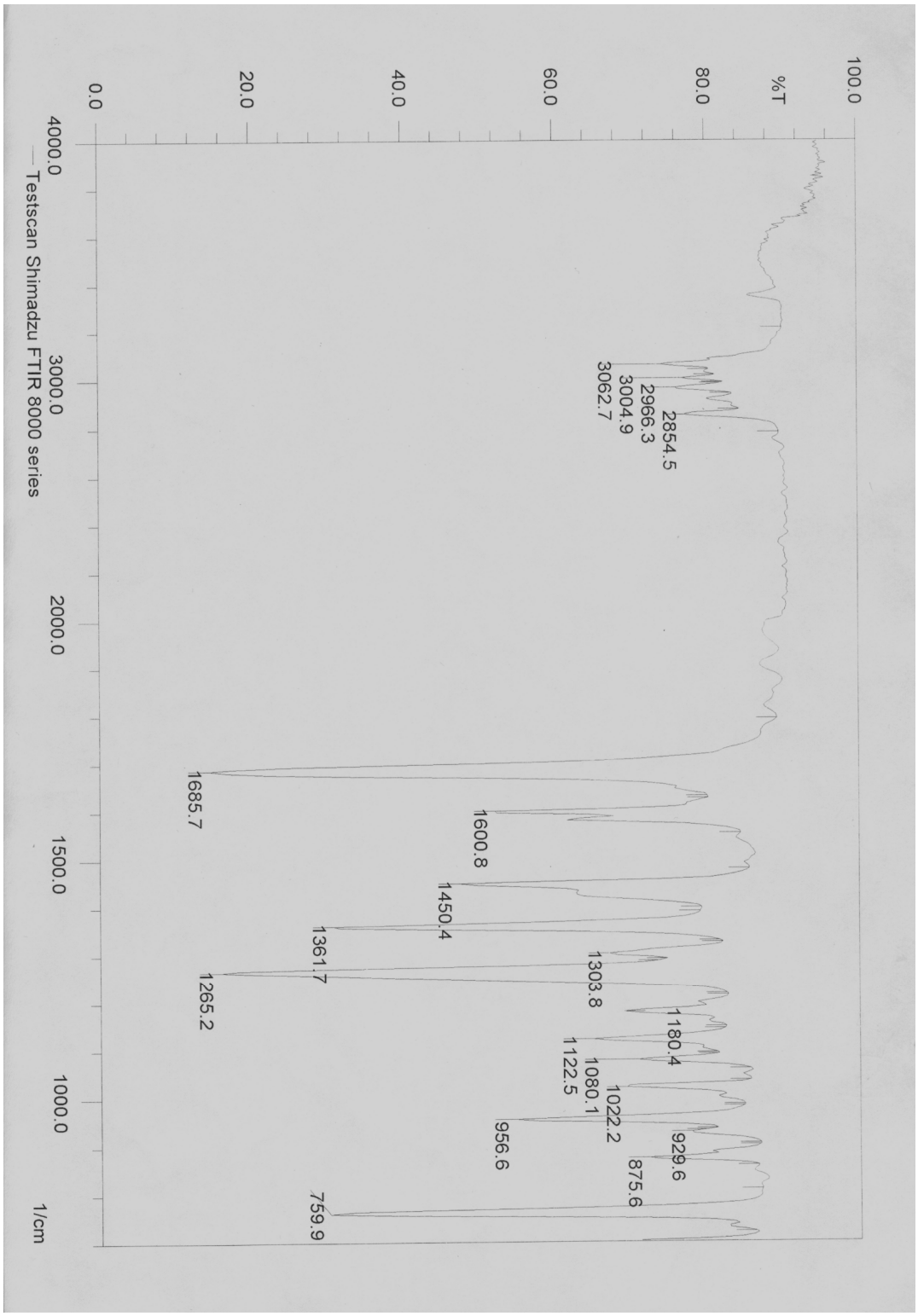


Fig A6: FTIR for α-Methoxy Cyclohexanone (20) from cyclohexanone methoxylation.



FigA7: FTIR for α-Hydroxy acetophenone (16) from hydroxylation of acetophenone.

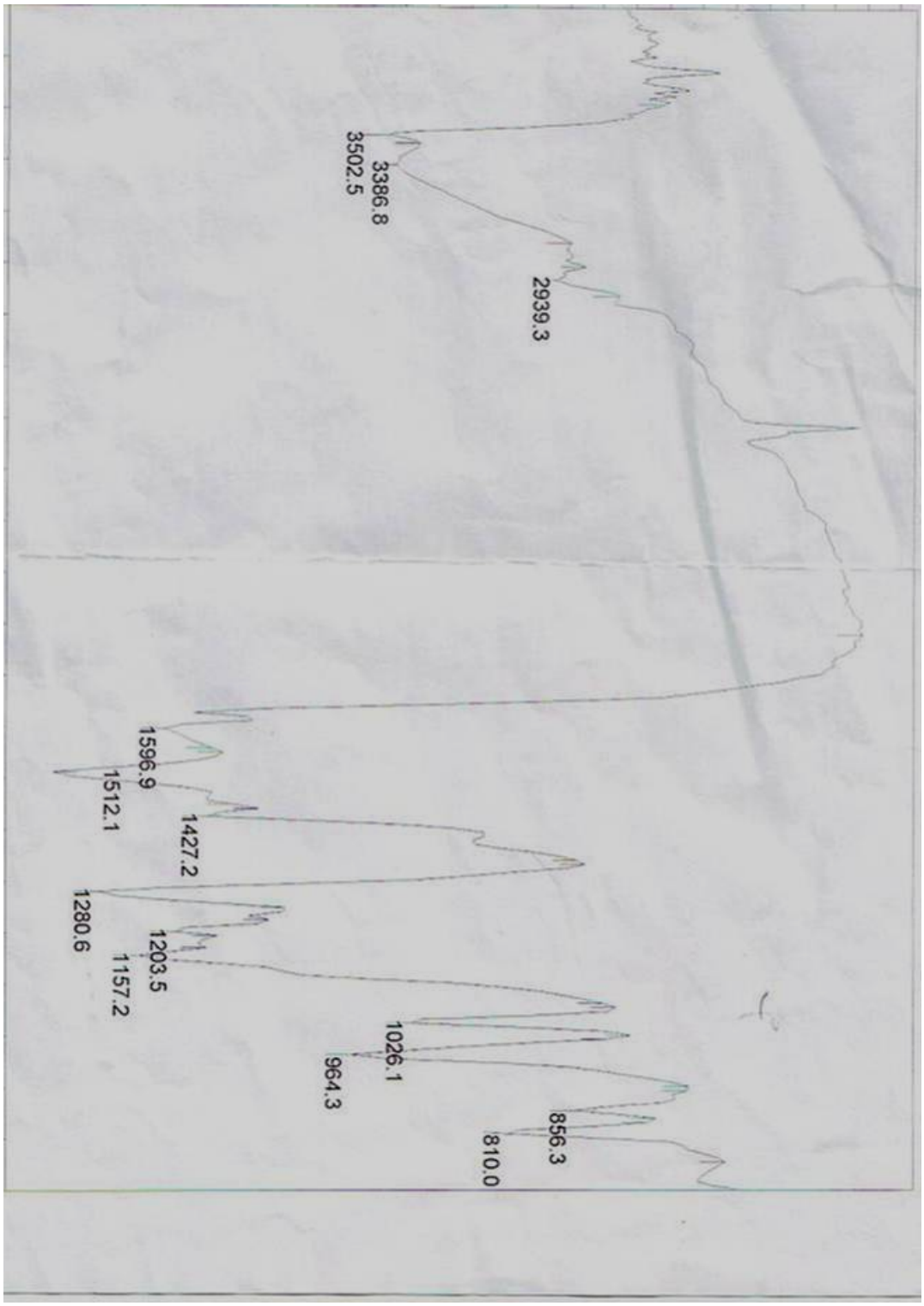


Fig A8: FTIR spectrum for Curcumin (6) extracted from turmeric

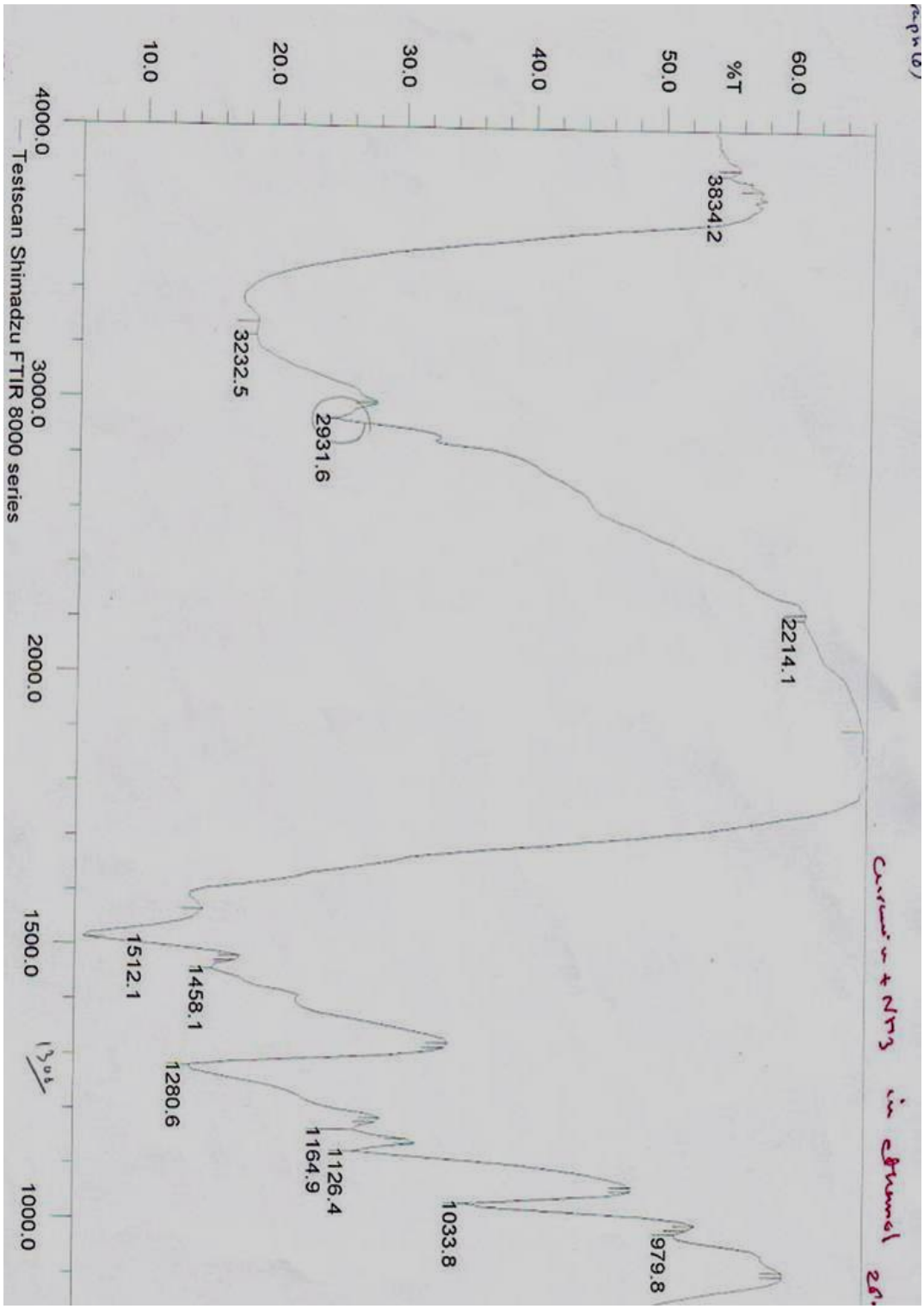


Fig A9: FTIR spectrum for (Curcumin +ammonia) extracted from turmeric

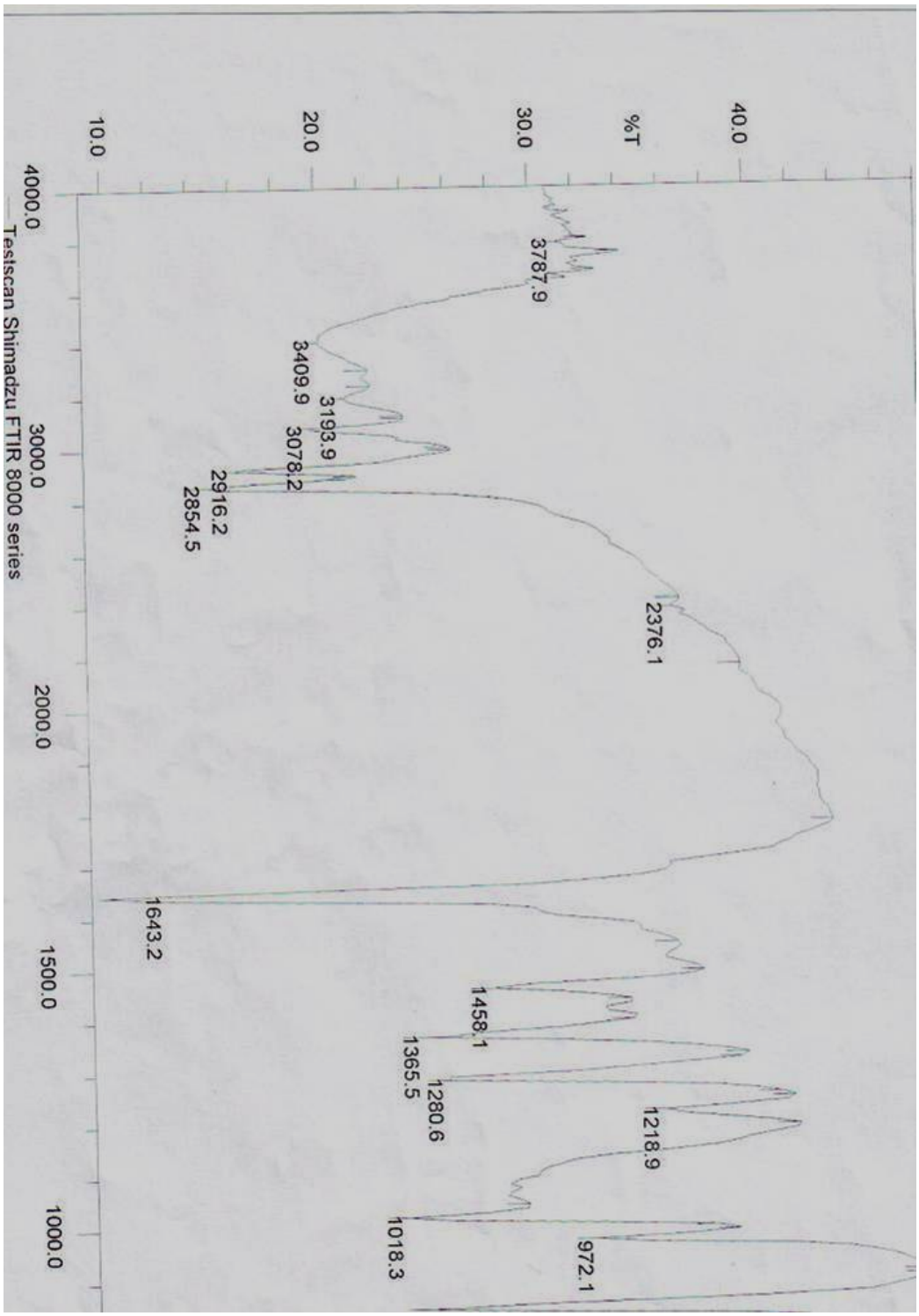


Fig A10: FTIR spectrum for Curcumin (6) extracted from turmeric

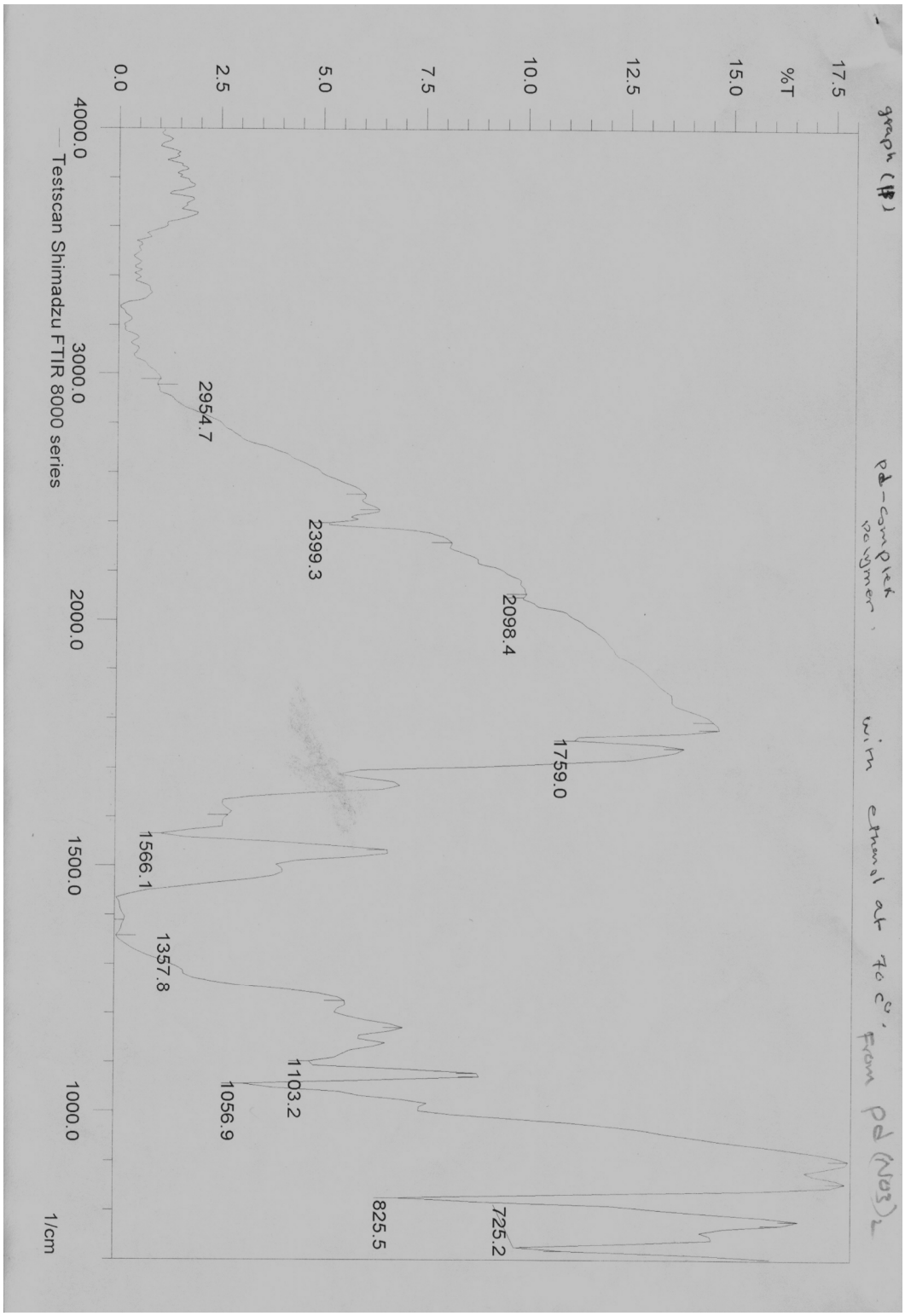


Fig A11: FTIR spectra for Pd-polyimine complex (12).

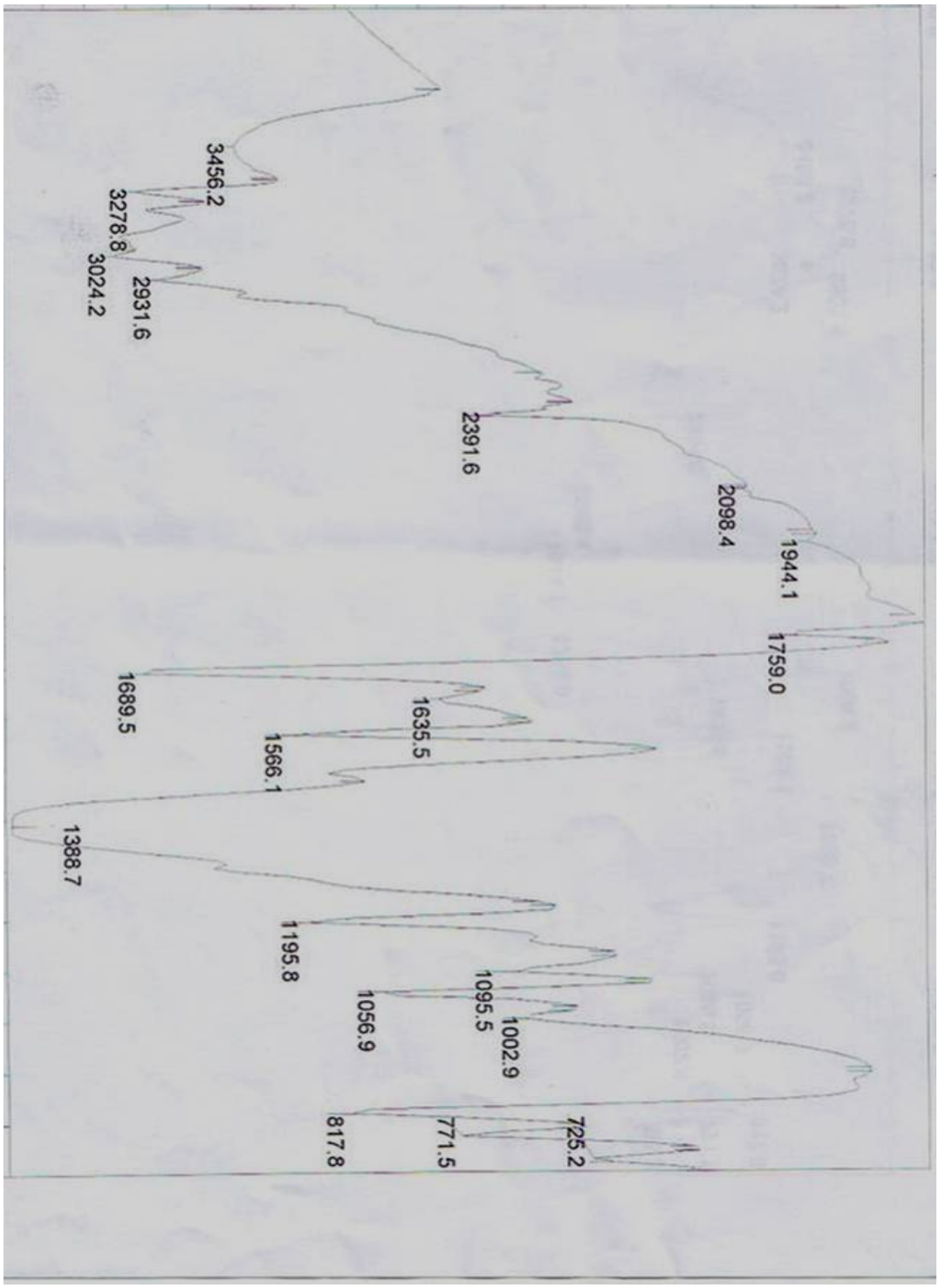


Fig A12: FTIR for Polyimine-Pd complex (12) before washing with ethanol.

Appendix B: NMR spectra for the prepared compounds.

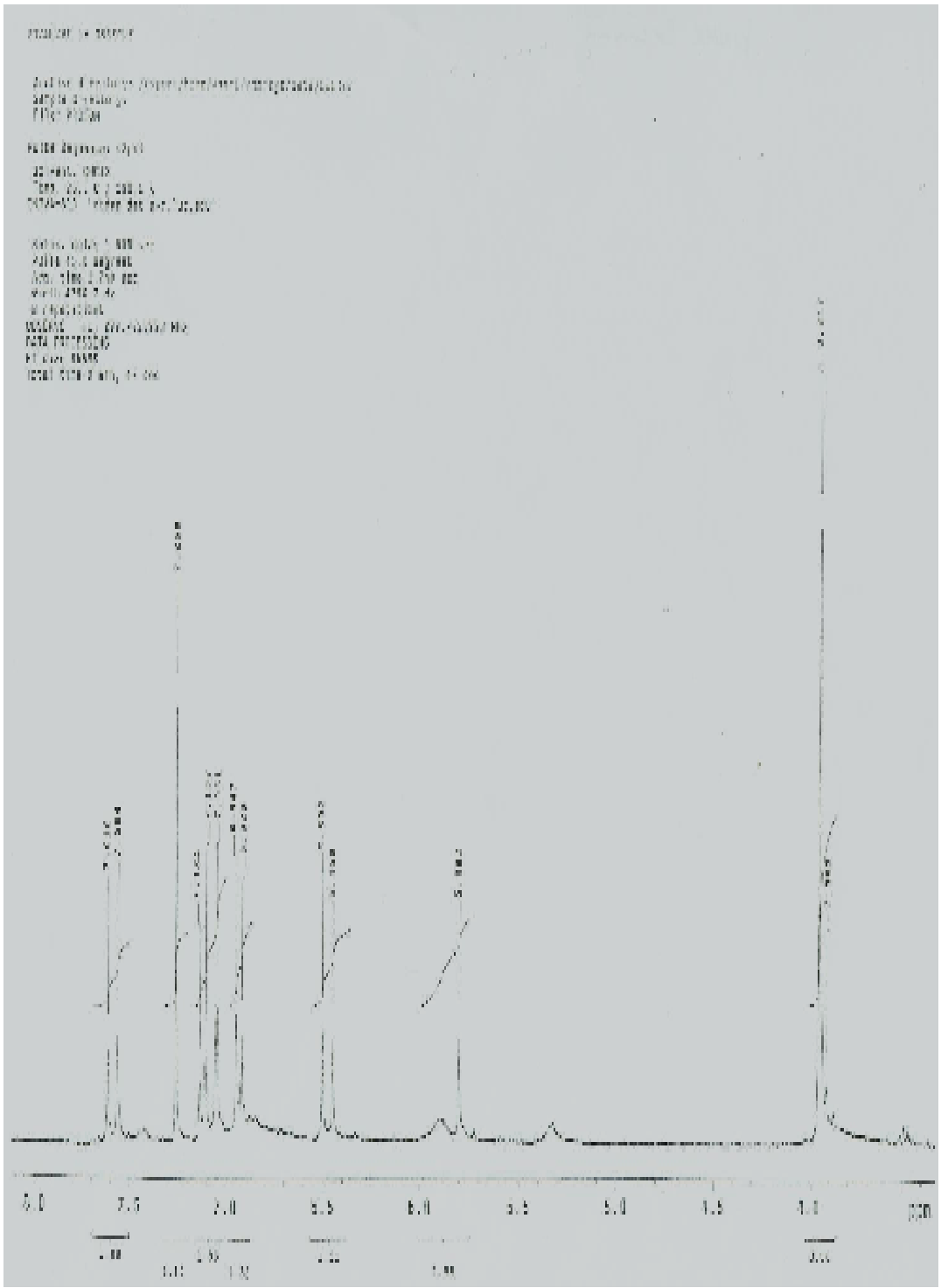


Fig B1: ^{1}H NMR for Curcumin (6) extracted from turmeric.

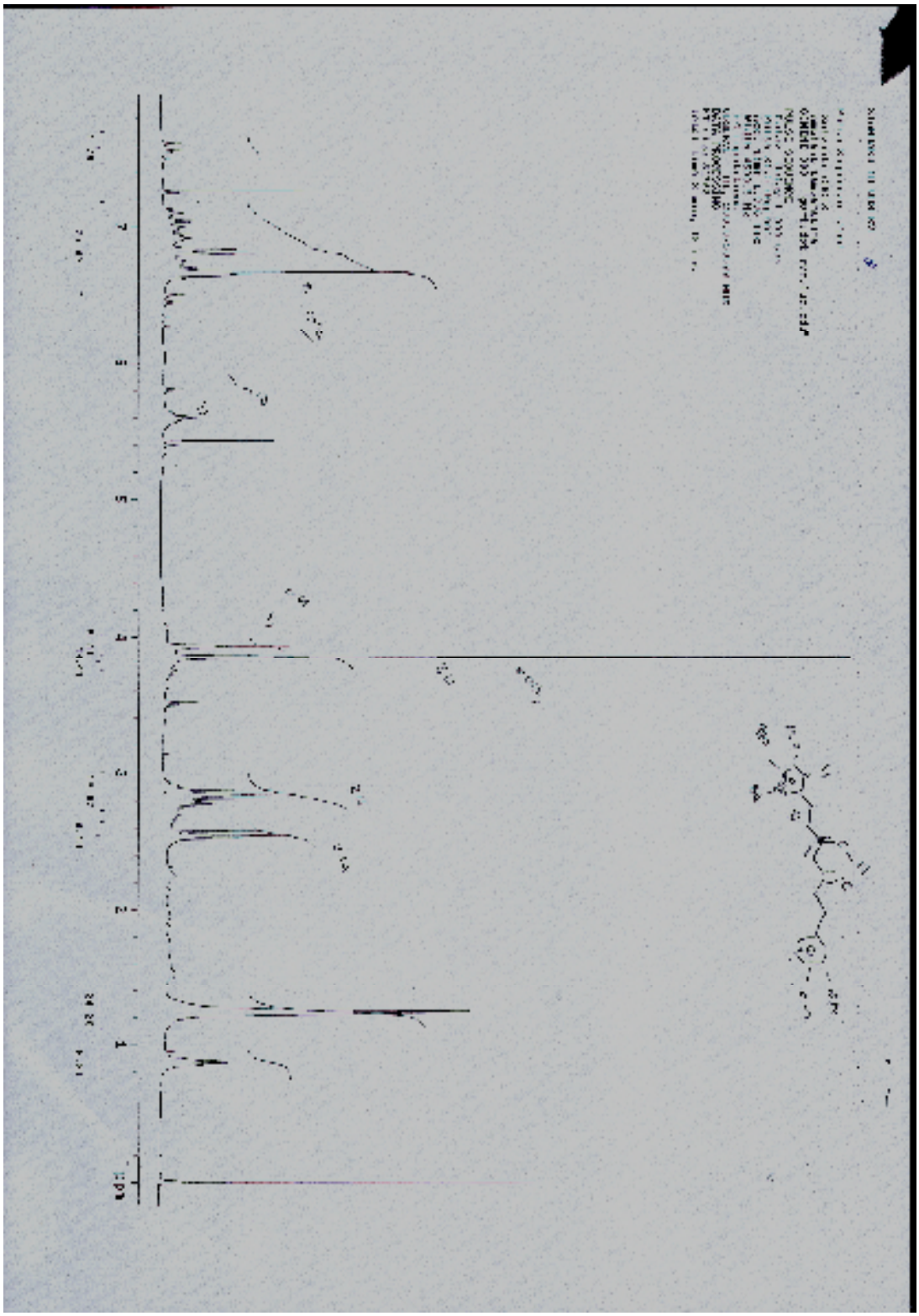


Fig B2: ^{1}H-NMR for Tetrahydrocurcuminoid (THC) (24).Using curcumin and Pd/H_2.

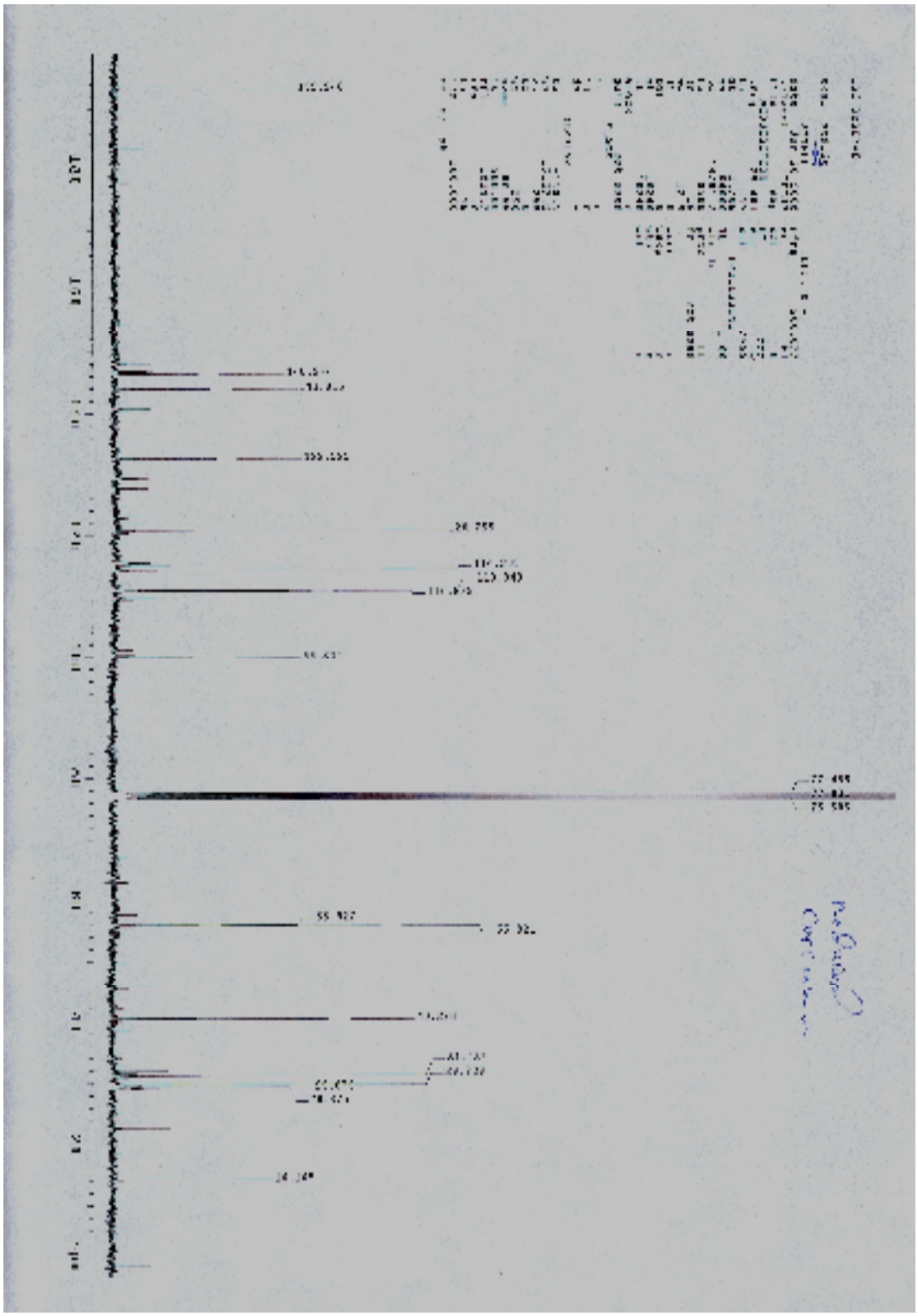
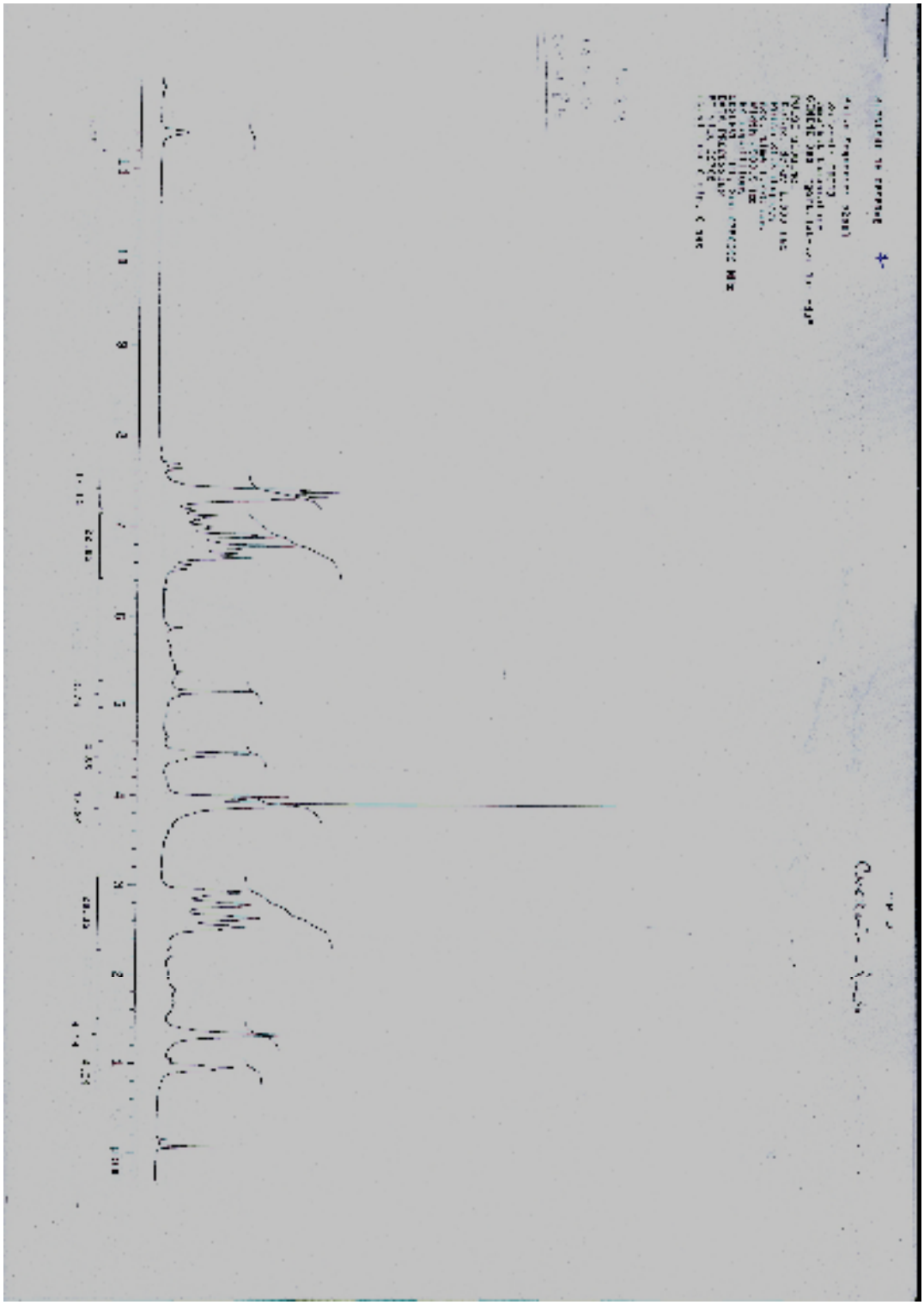


Fig B3: ^{13}C NMR for reduced curcumin (THC) (24) using Pd/H_2



FigB4: ^{1}H-NMR for Curcumin imine (THCDBI)(25) from THC and Dibenzylamine.

Fig B5: ^{1}H NMR for Pd- THCDBI Complex (26).

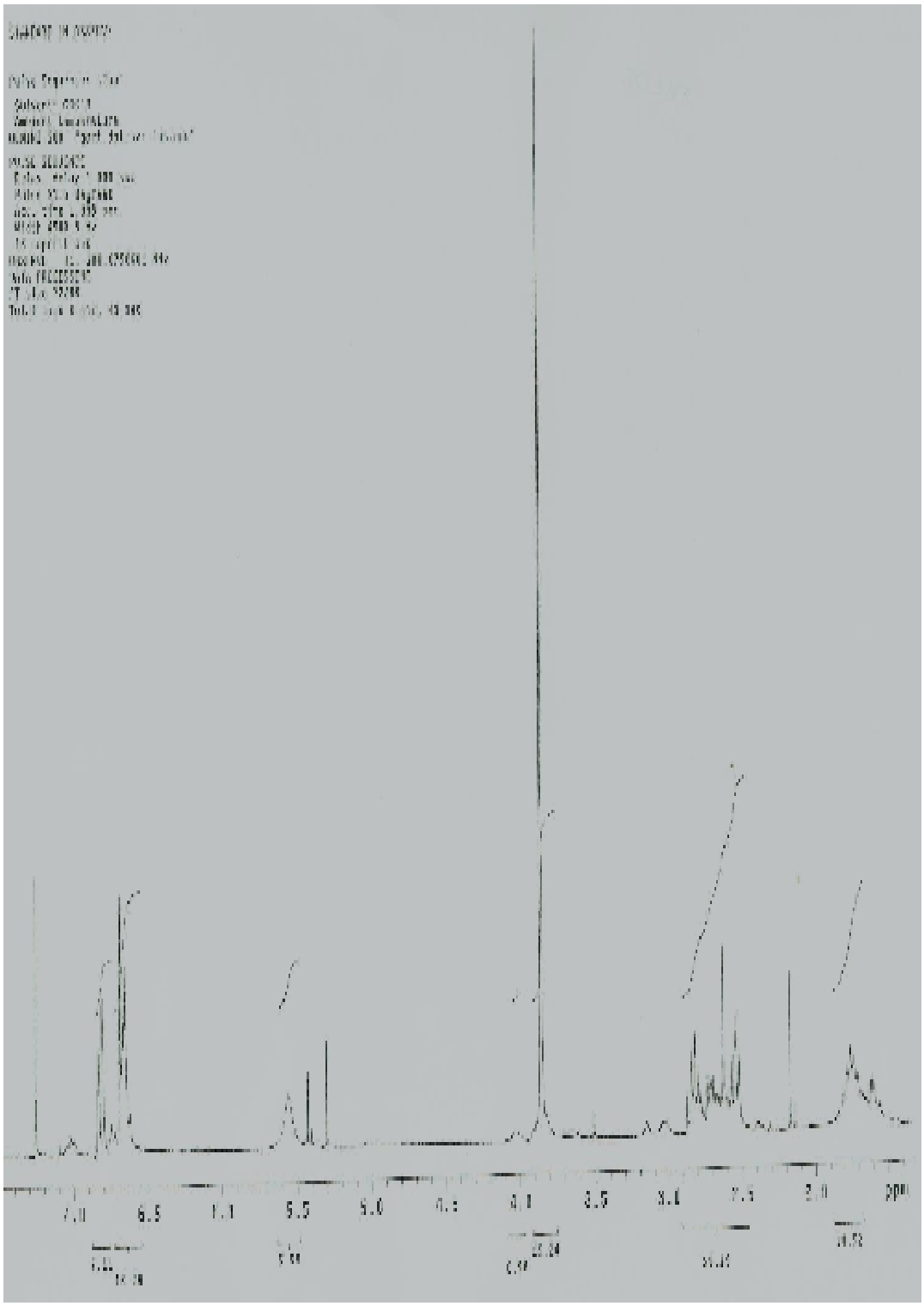


Fig B6: ^{1}H NMR for THCDI (27) from THC and Ammonia.

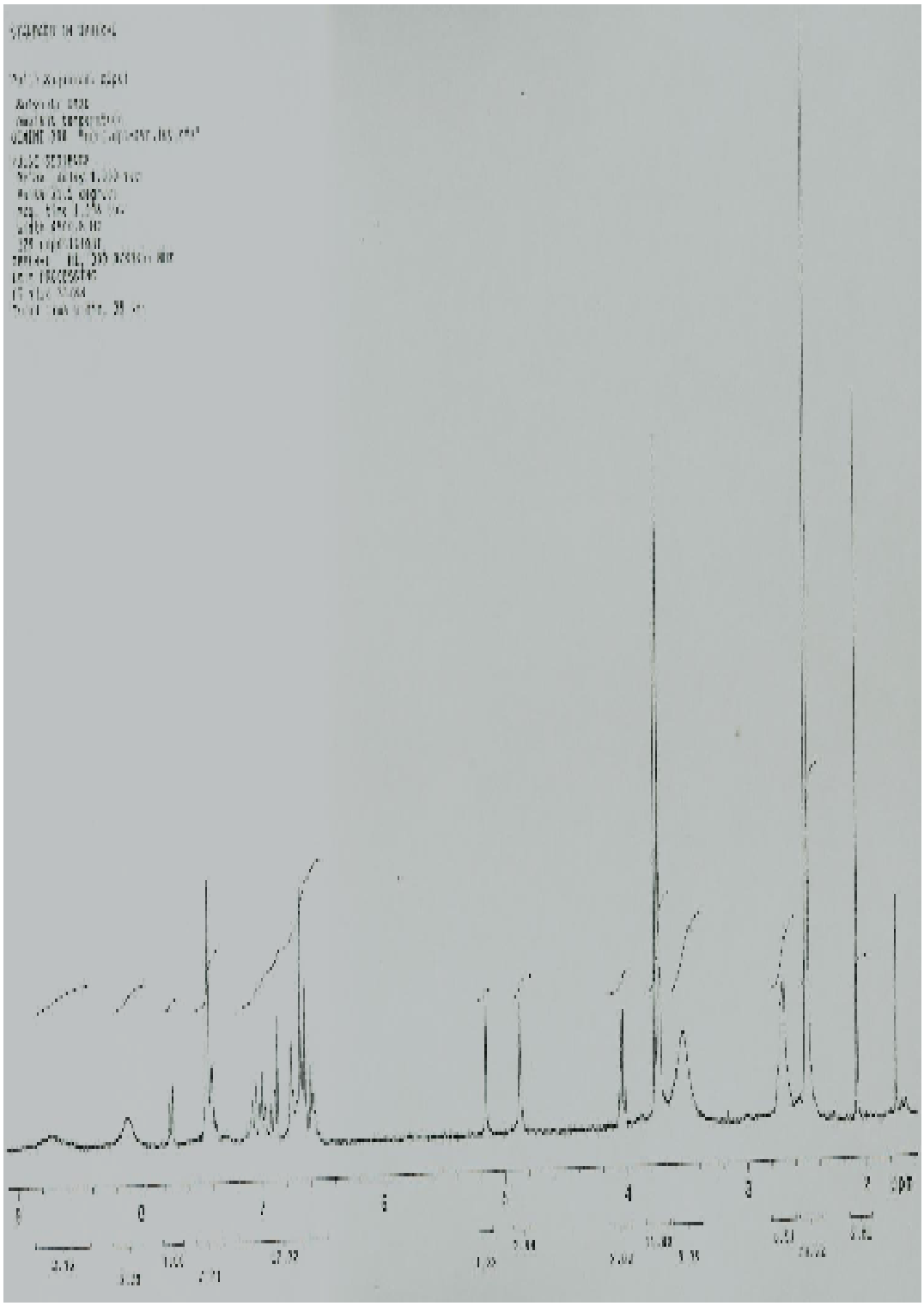


Fig B7: ^{1}H NMR for Pd- THCDI Complex (28).

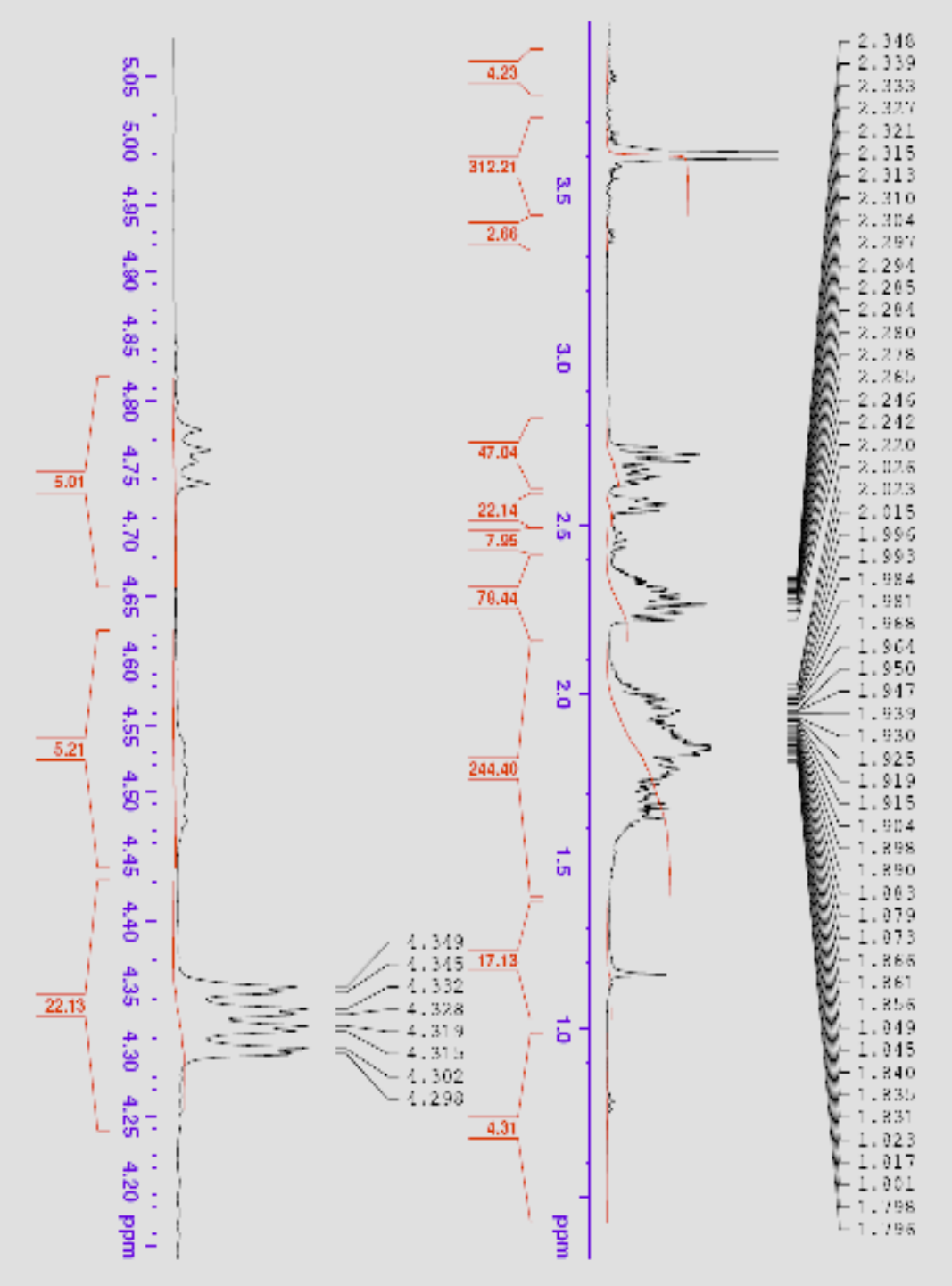


Fig B8: ^{1}H NMR for α-Hydroxy cyclohexanone(15) from hydroxylation of cyclohexanone in presence of polyimine – Pd (II) complex.

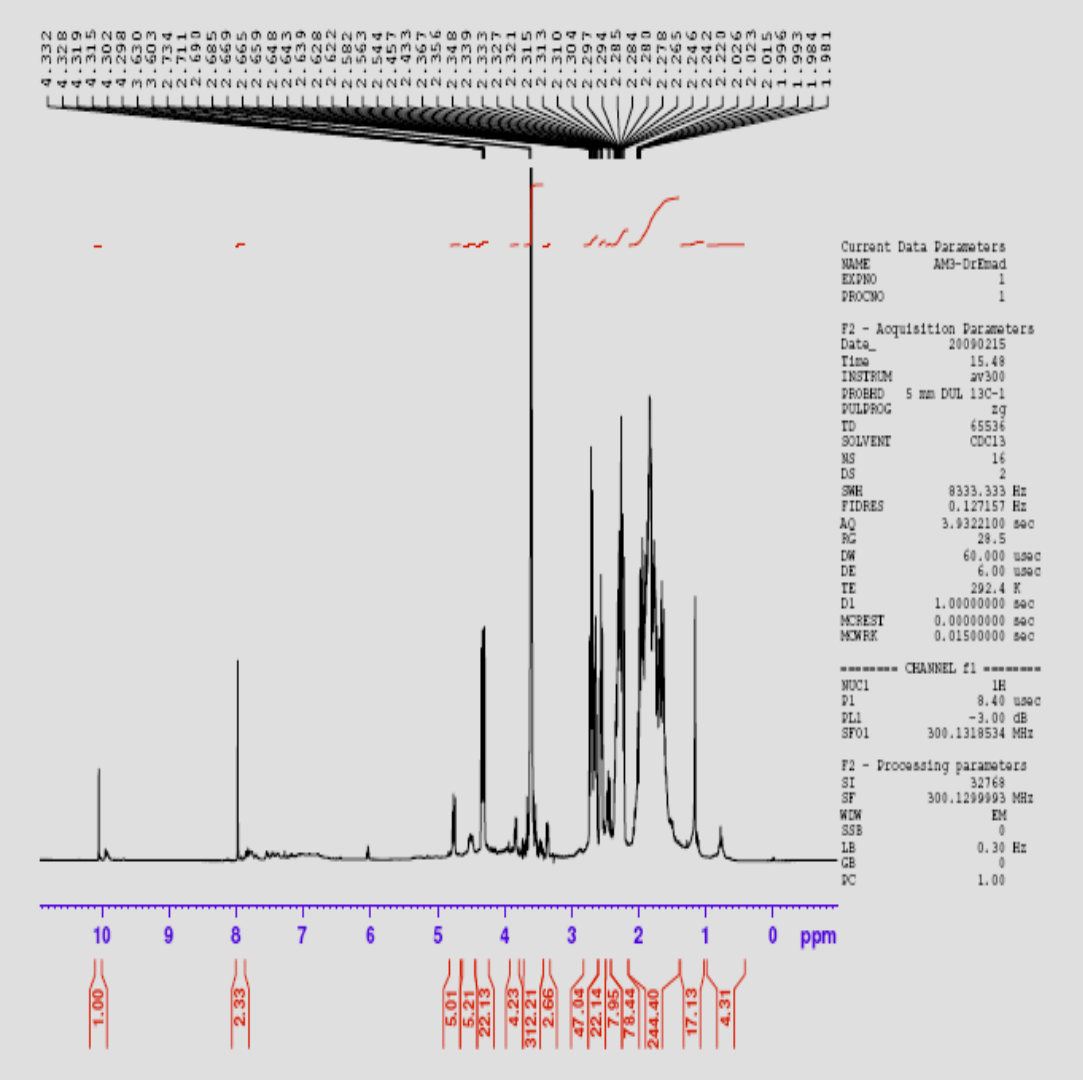


Fig B9: ^{1}H NMR for α- Hydroxy cyclohexanone (15) from hydroxylation of cyclohexanone in presence of polyimine-Pd(II) Complex.

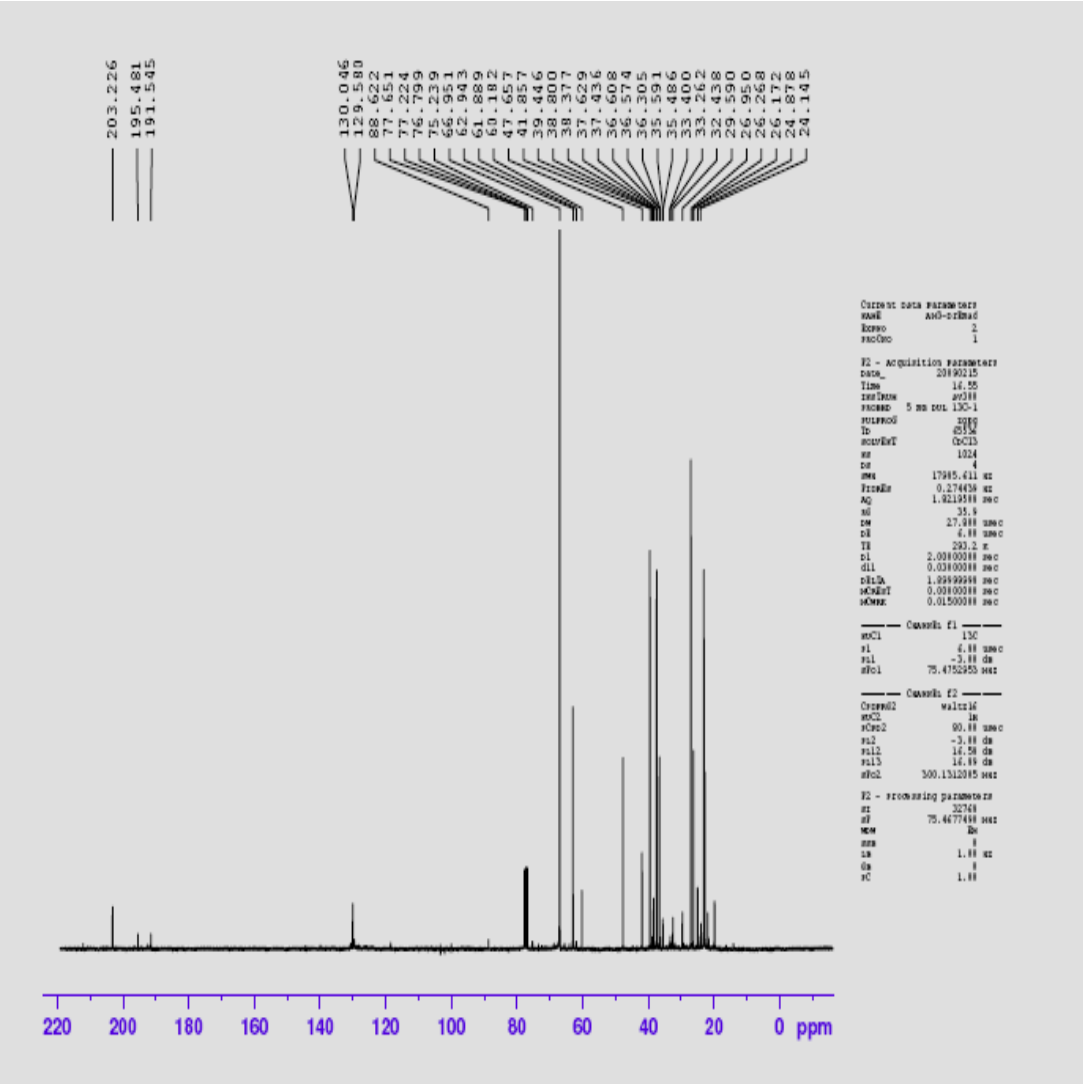


Fig B10: ^{13}C NMR for α-Hydroxy cyclohexanone (15) from hydroxylation of cyclohexanone in presence of polyimine-Pd(II) Complex.

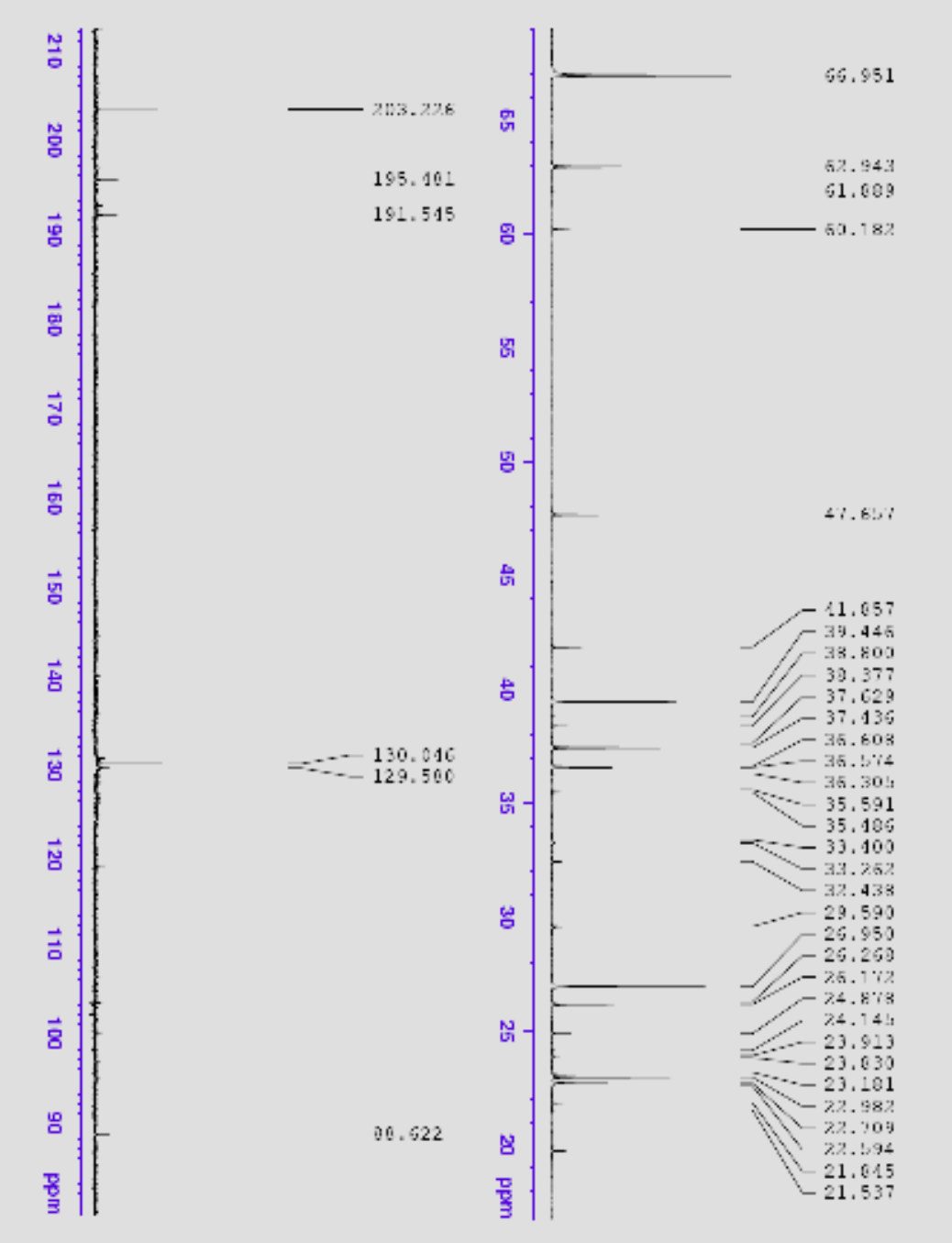


Fig B11: ^{13}C NMR for α-Hydroxy cyclohexanone (15) from hydroxylation of cyclohexanone in presence of Polyimine-Pd(II) Complex.

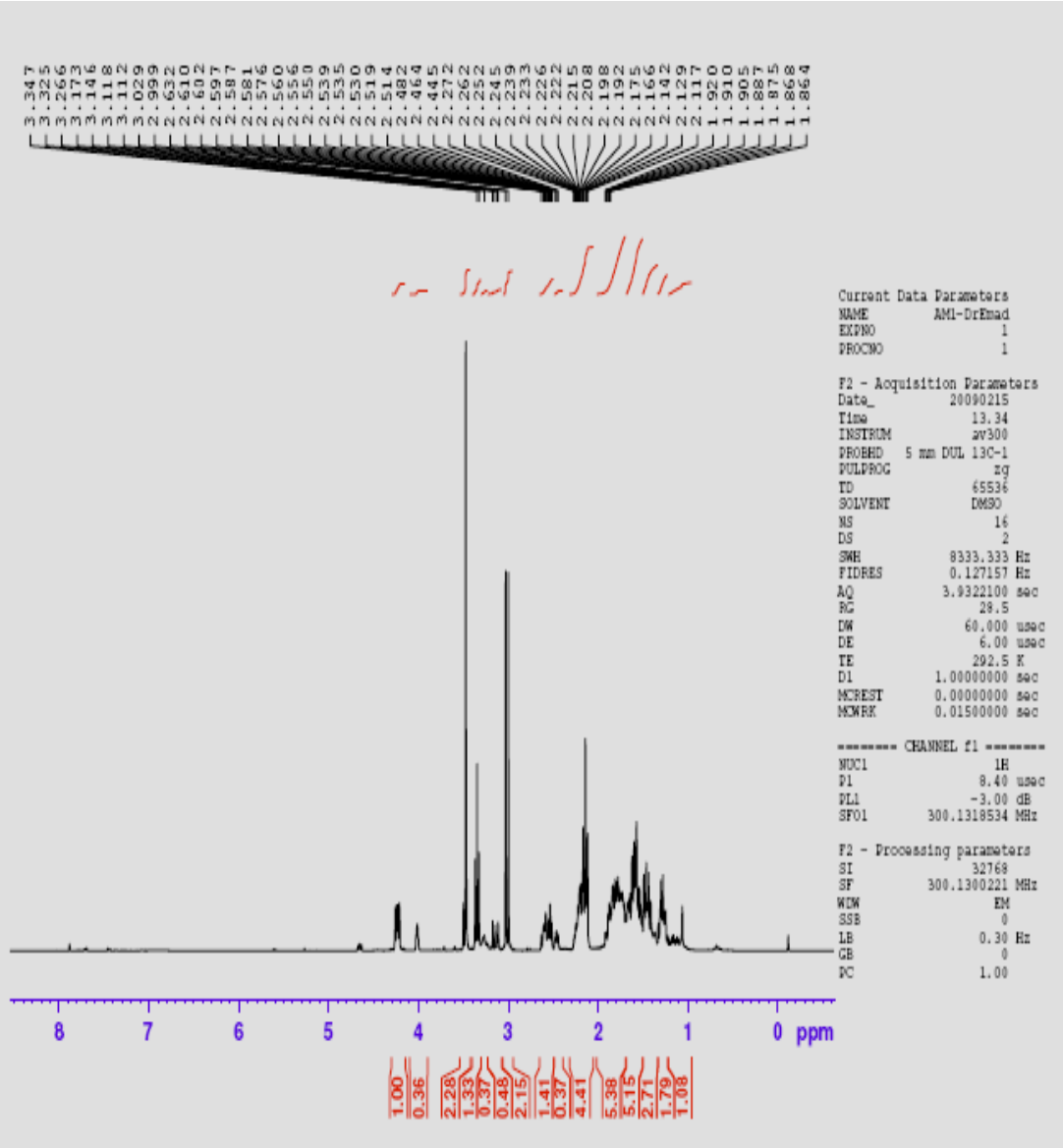


Fig B12: ^{1}H NMR for α-Methoxy cyclohexanone (20) from methoxylation of cyclohexanone in presence of Polyimine-Pd(II) Complex.

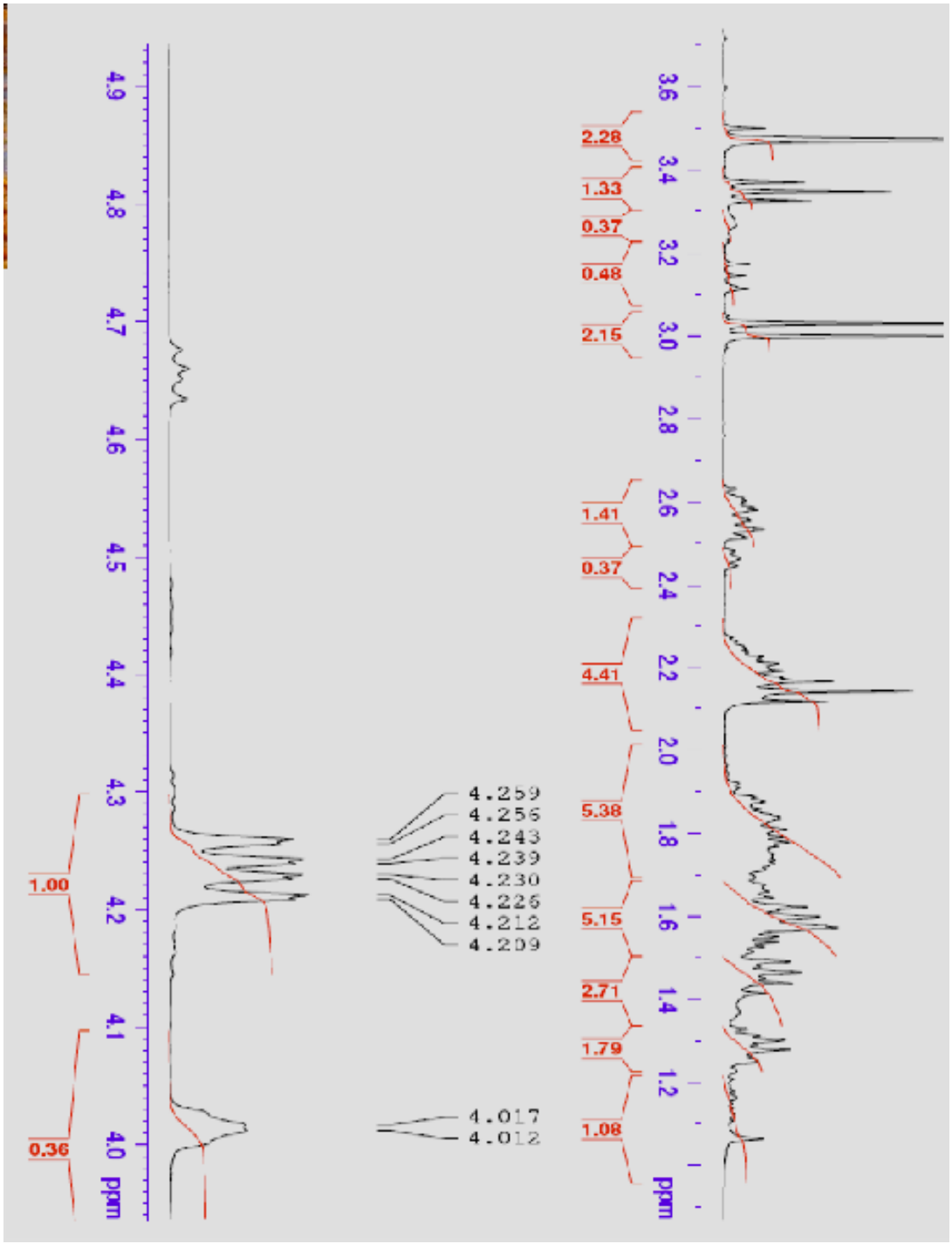


Fig B13: ^{1}H NMR for α-methoxy cyclohexanone (20) from cyclohexanone methoxylation in presence of Polyimine-Pd (III Complex.

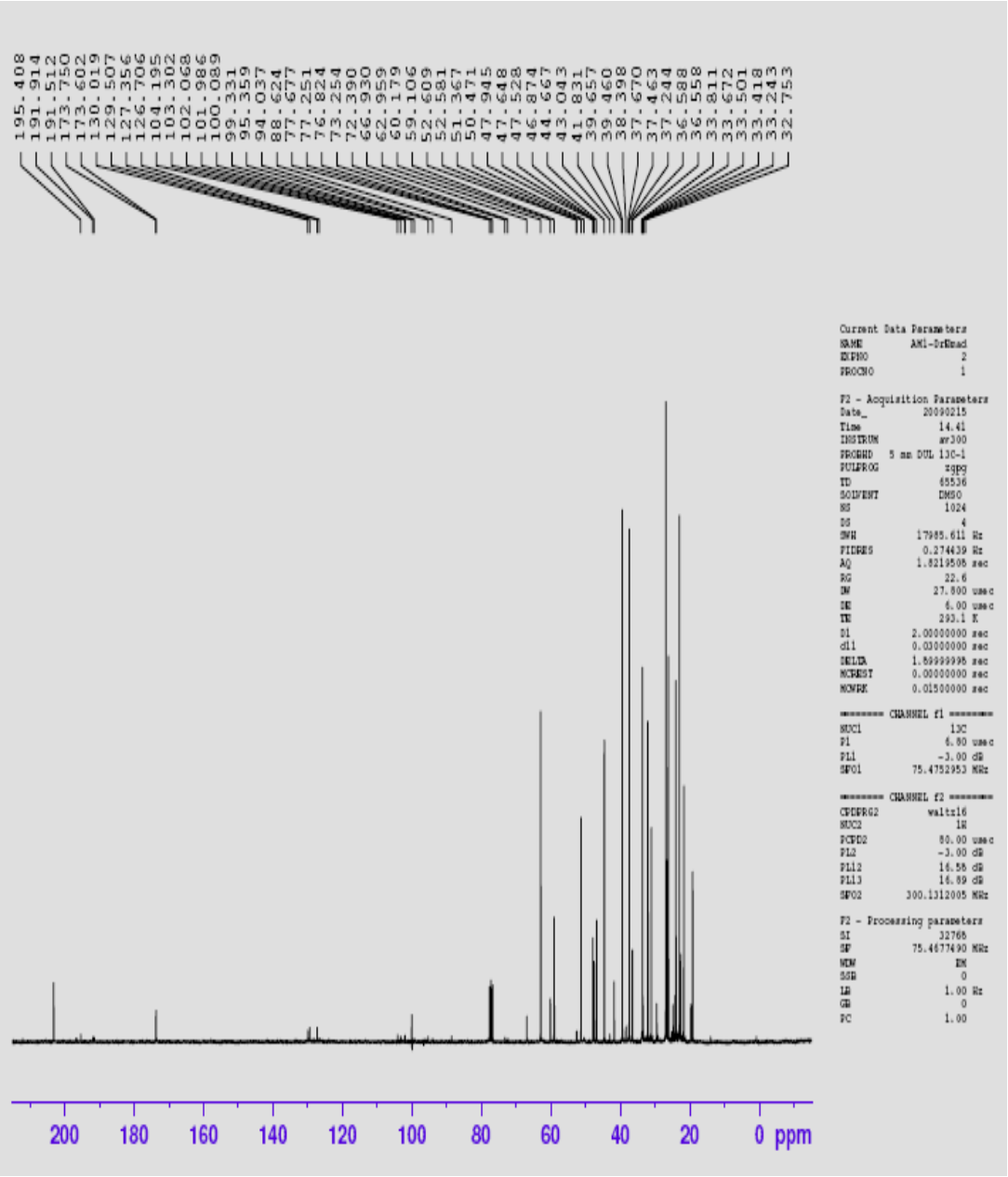


Fig B14: ^{13}C NMR for α-Methoxy cyclohexanone (20) from cyclohexanone hydroxylation in presence of Polyimine –Pd(II) Complex.

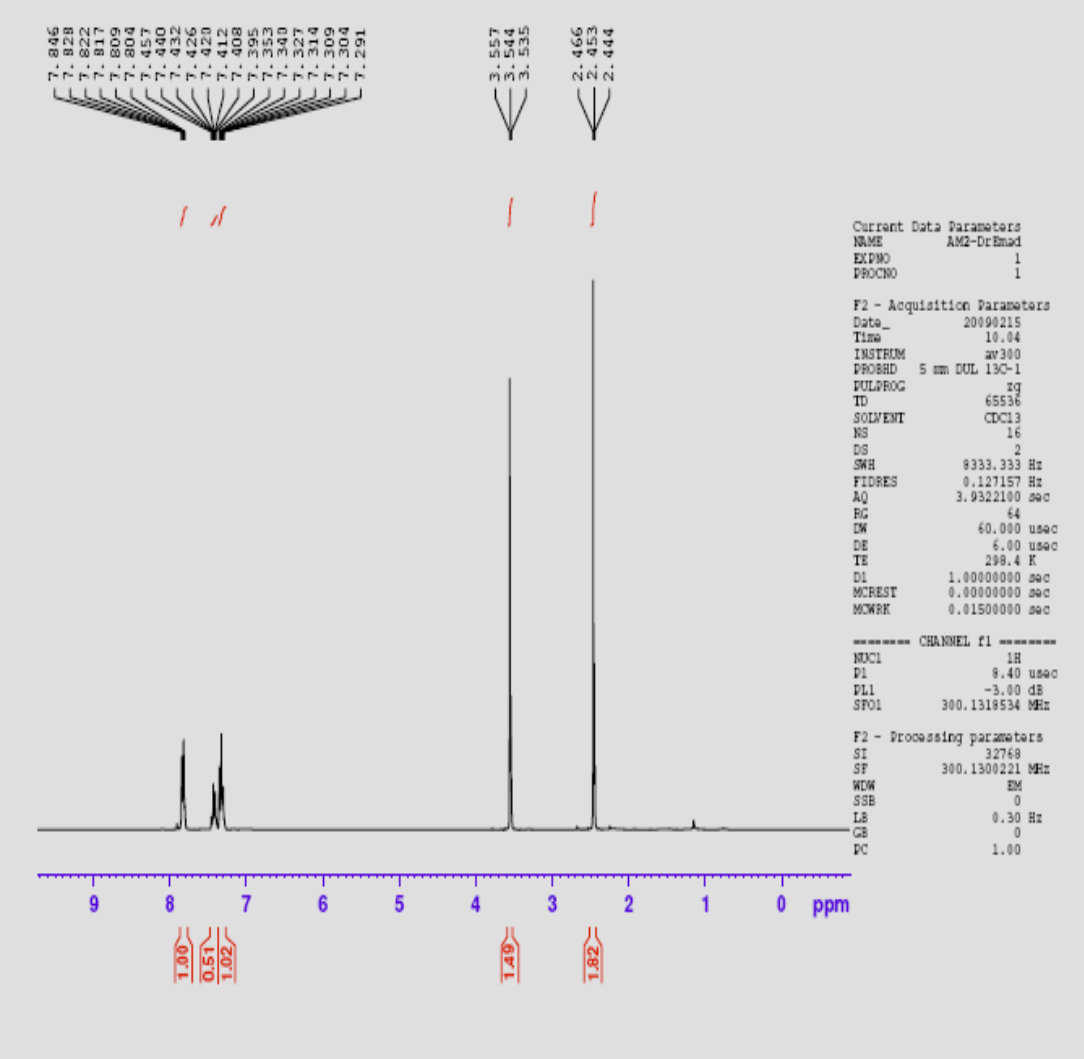


Fig B15: 1H NMR of 2-hydroxy acetophenone (16) obtained from hydroxylation of acetophenone.

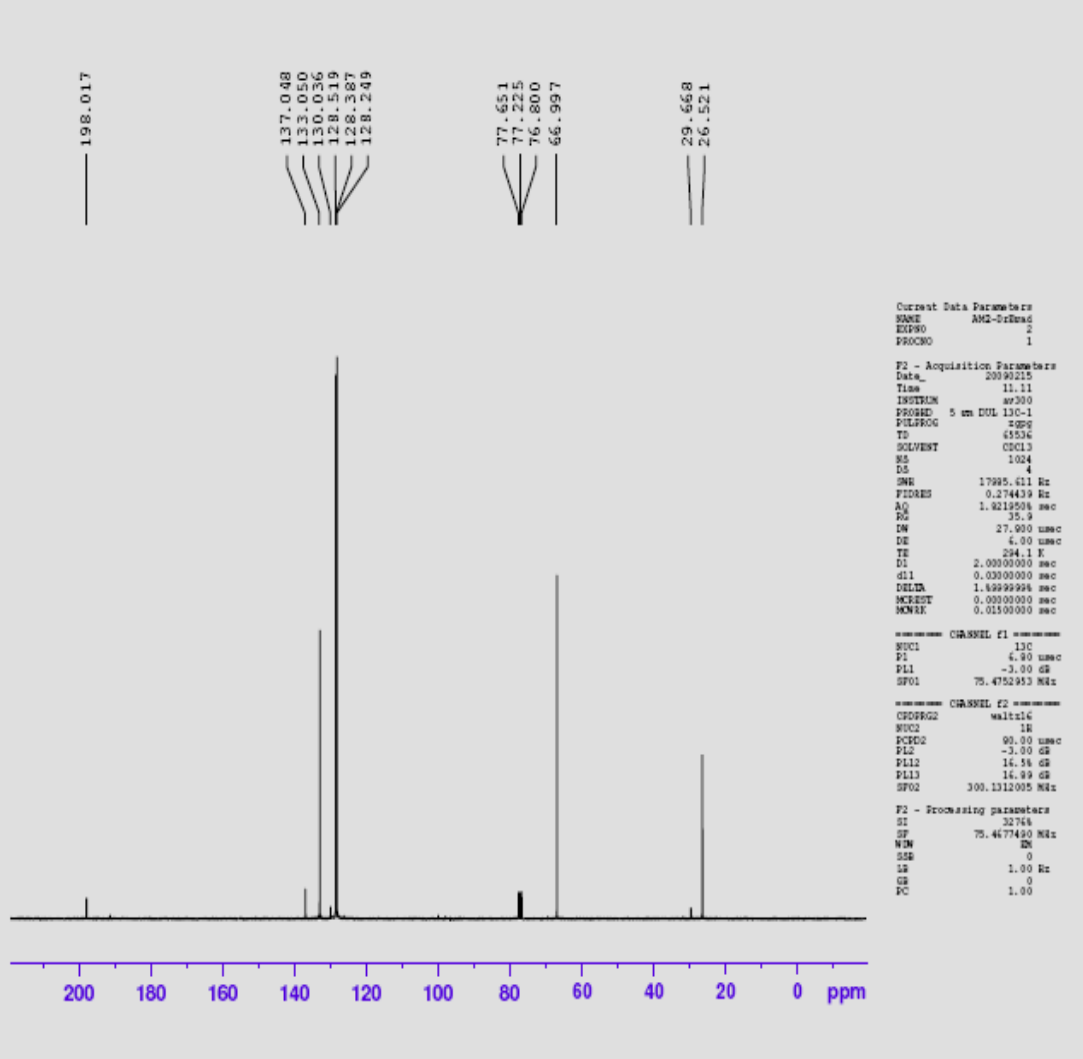


Fig B16: ^{13}C NMR for α-Hydroxy acetophenone (16) from hydroxylation of Acetophenone.

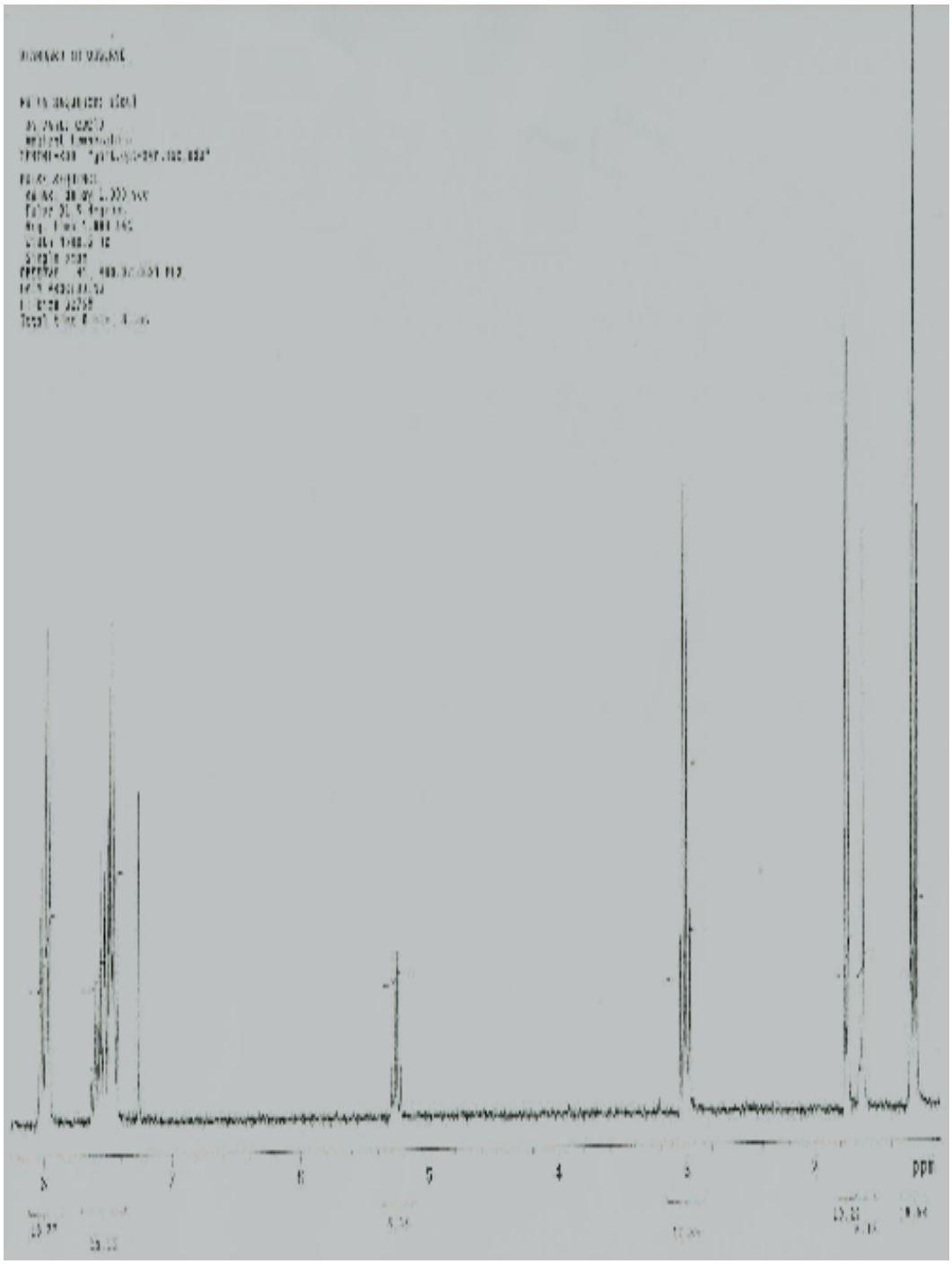


Fig B17: ^{1}H NMR for α-Hydroxy propiophenone (35) from propiophenone hydroxylation.

Appendix C: GC. Spectra for prepared compounds

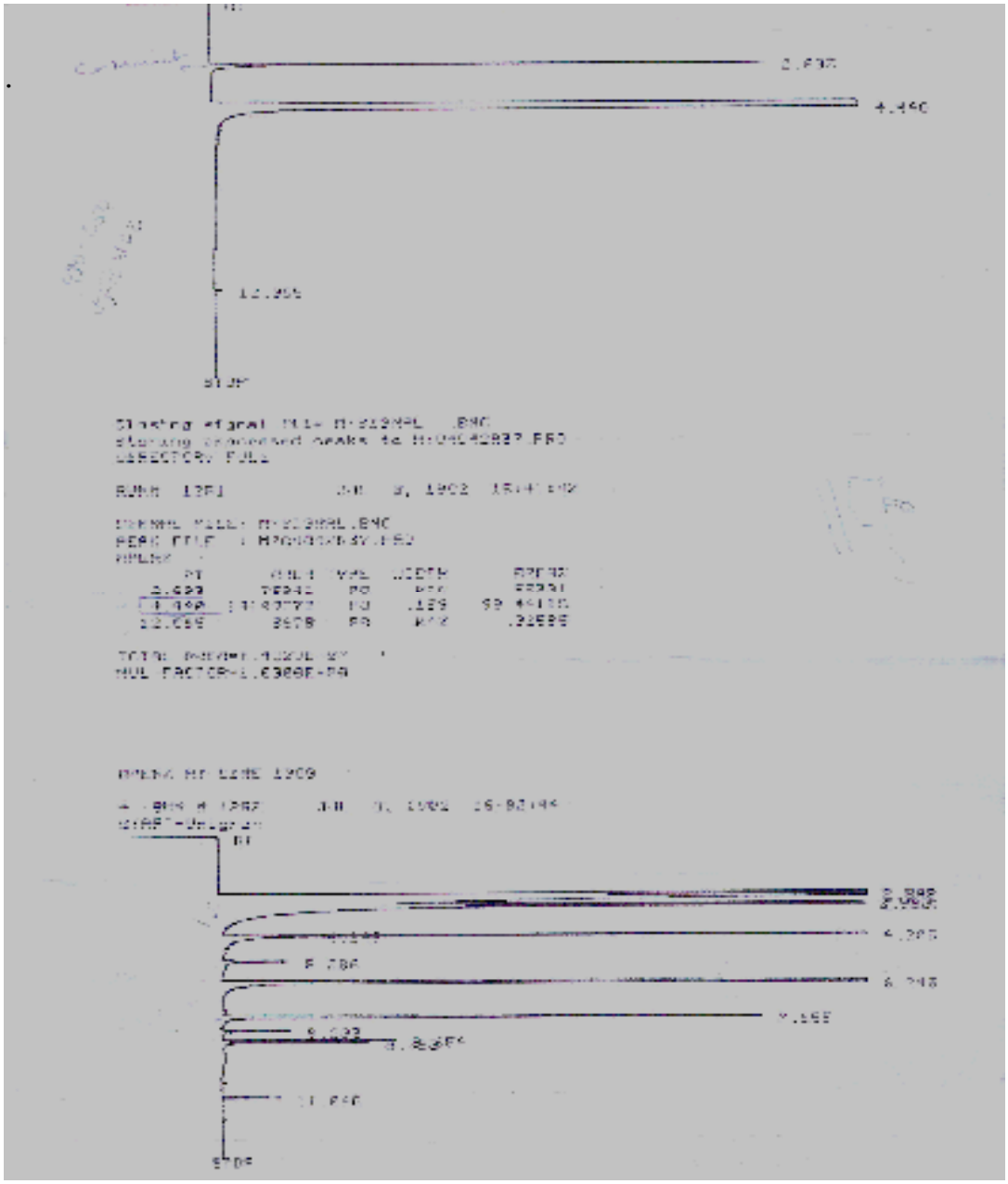


Fig C1: GC Spectra for α-Hydroxy cyclohexanone (15) from cyclohexanone hydroxylation.

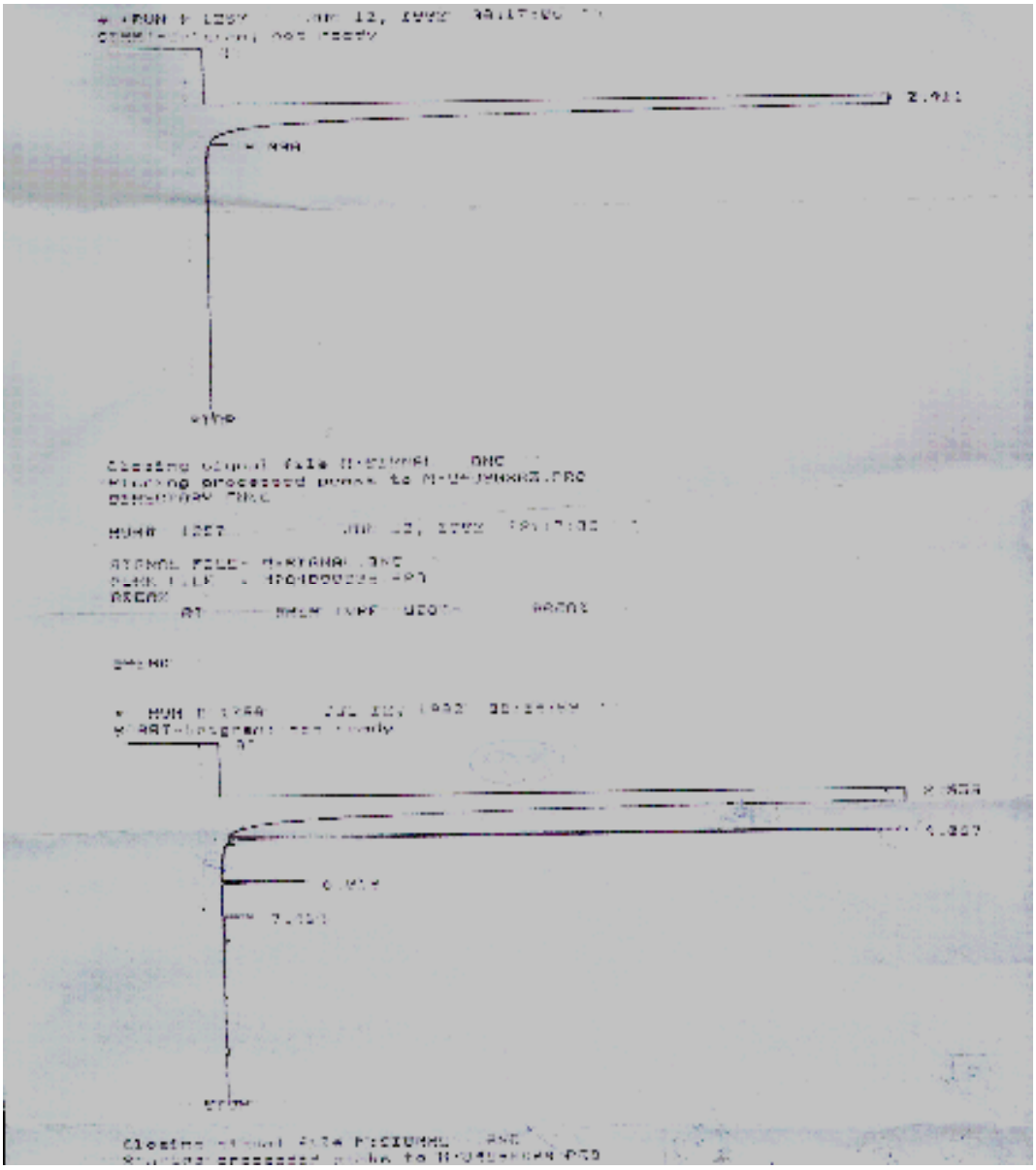


Fig C2: GC for α-Hydroxy acetophenone (16) obtained from hydroxylation of acetophenone.

جامعة النجاح الوطنية
كلية الدراسات العليا

استخدام العوامل المحفزة الطبيعية وغير الطبيعية مع عنصر البلاديوم لأكثر من مرة واحدة

إعداد
هشام عوض عبد شحادة

إشراف
د.عثمان حامد
د. وحيد الجندي

قدمت هذه الأطروحة استكمالا لمتطلبات الحصول على درجة الماجستير في الكيمياء بكلية الدراسات العليا في جامعة النجاح الوطنية في نابلس, فلسطين.
2009

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الملخص

تلعب العوامل الكيميائية المحفزة دورا مهما في التفاعلات الكيميائية, ونظرا لكثرة استخدامها وارتفاع تكاليفها كان لا بد من البحث عن بديل وبأثمان زهيدة. وفي هذا المشروع كان اهتمامنا البحث عن مصادر طبيعية. والمصدر الطبيعي الذي وقع عليه الاختيار هو مادة الكركم, وذلك لاستخلاص عامل محفز منه.

قمنا باستخلاص المادة الفعالة الأساسية منه باستخدام الايثانول, حيث أن التركيبة الكيميائية لها تحتوي على نوعين من المجموعات الوظيفية (مجموعتي كربونيل, وروابط ثنائية غير مشبعة). في الخطوة الأولى تم اختزال الروابط الثنائية وتحضير المركب(**THC**) **24**. في الخطوة الثانية تم مفاعلة المركب السابق(**24**) مع احد الامينات (ايثيلين ثنائي أمين) وتحضير المركب (**THCDBI**) **25**. بعد ذلك تم تثبيت أيون البلاديوم (Pd^{+2}) المحضر مسبقا عليه. مما أدى الى تحضير مركب معقد منه (**Pd-THCDBI**) **26**.

في الجزء الثاني من العمل تم أخذ المركب **24** ومفاعلته مع الامونيا وتحضير المركب (**THCDI**) **27**. باتباع طريقة التحضير في الجزء الأول حيث تم مفاعلة المركب **27** مع ايون البلاديوم فنتج المركب المعقد (**Pd-THCDI**) **28**.

أما في الجزء الثالث من العمل فقد قمنا بتحضير مبلمر معقد من مواد كيميائية تقليدية معروفة, للحصول على المبلمر المنشود (بولي إمين بلاديوم) **12** حسب الخطوات المذكورة في الجزء العملي, ولكن الفرق هنا أن الالدهايد (4,1- بنزين ثنائي كربوكسي الدهايد) **10**

المحضر هنا والمراد تحويله إلى المبلمر (البولي ايمين) **11** والذي تم مفاعلته مع البلاديوم لإنتاج الايون المعقد (بلاديوم بولي ايمين) **12**, ومن مميزات هذا المبلمر أن له أكثر من موقع فعال, وكذلك انه بالإمكان إعادة استخدامه في أكثر من حلقة حفزية.

في الجزء الأخير من العمل لقد تم اختبار الايونات المعقدة المحضرة على عدد من أنواع التفاعلات الكيميائية المعروفة مثل: (تفاعل هيك , كربنة الالفينات). حيث تم تحضير كل من: ألفا- هيدروكسي سايكلوهكسانون15, ألفا ميثوكسي سايكلوهكسانون 20 من سايكلوهكسانون, وكذلك ألفا-هيدروكسي اسيتوفينون 16 من اسيتوفينون باستخدام المبلمر المعقد رقم **12**, وهذه الطريقة أعطت نتائج جيدة, وذلك اعتمادا على النتائج المستخلصة من أجهزة التحليل الآلي, الكروماتوغرافيا GC, والأشعة تحت الحمراء IR والرنين المغناطيسي النووي NMR المستخدمة.

وكذلك تم استرجاع المبلمر المحفز المستخدم وتنظيفه وتنقيته باستخدام احد المذيبات العضوية وهو التولوين, ومن ثم أعيد استخدامه لأكثر من دورة حفزية, دون أن يخسر من فاعليته كثيرا.

وكذلك تم استخدام المركبين المعقدين **26** و **28** لتحضير المركبات التالية من مركباتها الأولية:

ألفا- هيدروكسي بروبيوفينون من بروبيوفينون(**35**).

ألفا- هيدروكسي سايكلوبنتانون من سايكلوبنتانون (**30**).

ألفا- هيدروكسي سايكلوهكسانون من سايكلوهكسانون (**15**).

6-ميثيل ,2- هيدروكسي سايكلوهكسانون(**32**).

وهذه المركبات بعد تحضيرها تم إثباتها باستخدام أجهزة التحليل الآلي السابقة الذكر.