CATALYTIC TRANSFER HYDROGENATION OF ORGANIC FUNCTIONAL GROUPS USING Ni, Ru COMPLEXES AND ASYMMETRIC INDUCTION USING RACEMIC CHIRAL AND ACHIRAL LIGANDS AND SYNTHETIC APPLICATIONS

A THESIS

SUBMITTED TO THE

UNIVERSITY OF PUNE

FOR THE DEGREE OF

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IN

CHEMISTRY

BY

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PUNE 411 008

SEPTEMBER 2005

CERTIFICATE

This is to certify that the work incorporated in this thesis entitled **"Catalytic transfer hydrogenation of organic functional groups using Ni, Ru complexes and asymmetric induction using racemic chiral and achiral ligands and synthetic applications"** submitted by **Mrs. Aruna Khair Sattar** was carried out by her under my supervision at **National Chemical Laboratory, Pune 411 008.** Material that has been obtained from other sources is duly acknowledged in the thesis.

Date:

Research Guide

(Dr. Suresh Iyer)

DECLARATION

I hereby declare that the thesis entitled **"Catalytic transfer hydrogenation of organic functional groups using Ni, Ru complexes and asymmetric induction using racemic chiral and achiral ligands and synthetic applications"** submitted for the **degree of Doctor of Philosophy** to the **University of Pune**, under the guidance of **Dr. Suresh Iyer**. The work is original and has not been submitted in part or full by me for any degree or diploma to this or any other University.

Date:

(Research Student)

Mrs. Aruna K. Sattar

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Life offers very few occasions, that you wish to celebrate with all near & dear ones, the ones who matter, I deeply and sincerely acknowledge and invite you to add to the spirit of the occasion.

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I gratefully acknowledge the presence of Almighty God for his kind benedictions & Blessings by his unseen hands, though his presence was all around through my study.

Most importantly, I raise my eyes to my Late Father who, raised me, supported me, loved me and taught me to manifest the fullness of my talents while making a difference in the lives of all those around us !! To him I dedicate this thesis.

Finally, I thank CSIR and DST for financial assistance and the Director, NCL, Pune for providing necessary facilities to complete my work successfully.

Aruna K. Sattar

List of Publications

- $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation using $HCOONH_4$

  Suresh Iyer, Aruna K. Sattar, Synth. Commun., 1998, 28 (10), 1721.

- Novel Ligands and Ru catalysts, Ru DAB, Salen and DMSO complexes catalyzed selective transfer hydrogenation of ketones and aldehydes

  Suresh Iyer, Aruna K. Sattar, Ind. J. Chem., 2003, 2805.

- Transfer hydrogenations catalyzed by {Ni (II)}, $NiCl_2\{P(C_6H_5)_2\}_2$ and {Ni (0)}, $Ni\{P(OC_6H_5)_3\}_4$ and $RuCl_2\{DMSO\}_4$ - Racemic ligands in asymmetric induction

  Suresh Iyer, Aruna K. Sattar (Paper communicated, 2005).

- Nitrogen ligands - The transition metal catalyzed reaction of aryl halides with olefins (Mizoroki-Heck), phenylboronic acid (Suzuki coupling) and (Buchwald-Hartwig) amination, new catalysts and effect of co-catalysts - Aryl halide activation - Part - 1

  Suresh Iyer, Girish M. Kulkarni, C. Ramesh & Aruna K. Sattar. (Paper accepted in Ind. J. Chem, 2005).

CONTENTS

Chapter - 3 Asymmetric transfer hydrogenation with racemic ligands

- Introduction
- Result and Discussion
- Conclusion
- Experimental
- References

GENERAL REMARKS

1. All melting points and boiling points are uncorrected.
2. All temperatures are recorded on centigrade scale.
3. Numbers given to charts, figures and structures in each chapter of the thesis refer to that particular chapter only. The references and spectra are given at the end of each chapter.
4. A brief summary of each chapter is given at the beginning of that chapter.
5. All the solvents were distilled before use. Petroleum ether refers to the fraction boiling in the range 60-80°.
6. TLC analyses were carried out on glass plates with a mixture of silicic acid and plaster of Paris (85:15, 200-300 mesh) and activated at 120° for 3 hr. Solvent systems used were pet.ether, benzene, ethyl acetate and chloroform or a suitable mixture of two or more of these solvents depending upon the nature of the compound. The plates were developed by keeping in an iodine chamber or by spraying with sulphuric acid.
7. Unless otherwise stated, all solutions were dried over anhydrous sodium sulfate.
8. Unless otherwise stated, all b.ps. refer to the bath temperature.
9. The infrared spectra of liquid were recorded as liquid films and that of solids as nujol mulls on a Perkin-Elmer infracord spectrophotometer model 137-B and 1620 FT-IR and on Perkin-Elmer infracord spectrophotometer model 599-B using sodium chloride optics. IR bands are express in ν cm^{-1}.

10. ^{1}H-NMR spectra were recorded using TMS as internal reference on Bruker AC=200, Bruker MSL-300-500 instruments using $CDCl_3$ as solvent. Chemical shifts are reported in δ units.

11. In the description of PMR signals, the abbreviations d, t, q, m, br s, br d means doublet, triplet, quarter, multiplet, broad singlet and broad doublet respectively.

12. Column chromatography was carried using silica gel (60-120 mesh), which was activated at 125-130°C for 3 hr.

List of Abbreviations

Ac	Acetyl
Ar	Aryl
aq	Aqueous
BINAP	(1,1'-binaphthalene-2,2'-diylbis diphenyl)-phosphane
Boc	tertiary butyloxy carbonyl
b.p.	boiling point
Bu^n	n-butyl
CAN	Cerium Ammonium Nitrate
cat	Catalyst
CBZ	benzyloxy carbonyl
Co-cat	co-catalyst
COD	Cyclooctadiene
Cy	Cymene
DAB	Diazabutadiene
°C	degree centigrade
DCM	Dichloromethane
DMSO	Dimethylsulfoxide
DMF	N,N-dimethyl formamide
Dpen	diphenyl ethylene diamine
ee	enantiomeric excess
FG	functional group

g	Gram
h	Hour
i-PrOH	Isopropanol
IR	Infrared
KtBuO	Potassium tertiary butoxide
L	Ligand
M	Metal
M	Molar
min	Minute
ml	Milliliter
mmol	Millimole
mp	melting point
NOBIN	2-amino-2’-hydroxy-1,1-binaphthyl
NOMBIN	2-amino-2’-methoxy-1,1-binaphthyl
NMP	N-methyl pyrrolidone
OAc	Acetate
OMe	Methoxy
PPh_3	triphenyl phosphine
Ph	Phenyl
rt	Room temperature
S	Substrate
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography

TMS	trimethyl silane
Ts	Tosyl
TsDPEN	N-(para-toluene sulfonyl)-1,2-diphenyl ethylene diamine
TsEN	N-(para-toluene sulfonyl)-1,2-ethylene diamine

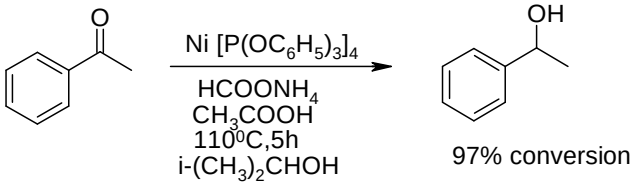
ABSTRACT

Chapter - 1

Nickel catalyzed transfer hydrogenation $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation using ammonium formate and $i\text{-}(CH_3)_2CHOH$

Catalytic transfer hydrogenation has found widespread use in organic synthesis. Use of $HCOONH_4$ as transfer hydrogenating agent with Pd/C as catalyst has been reported in recent years. Raney Ni has also been used as a catalyst for reduction of hydrazones and azides using $HCOONH_4$. This combination of Pd/C and $HCOONH_4$ is effectively used in the reductive ring opening of epoxides. $Pd\{P(C_6H_5)_3\}_4$ has also been used for transfer hydrogenation of organic functional groups. $NiCl_2\{P(C_6H_5)_3\}_2$ catalyzed the transfer hydrogenation of aldehydes and ketones using isopropyl alcohol with NaOH/ KOH as co-catalyst.

Scheme - 1



Ni (0) catalyst are known to cause isomerisation forming NiH complex, which is the active species. $Ni\{P(OC_6H_5)_3\}_4$ was used, therefore, the oxidative addition to $HCOONH_4$ forming NiH, which could then cause the reduction of organic functional group. This is the first example of a homogenous catalyst Ni (0) being active for the catalysis of the transfer hydrogenation using $HCOONH_4$ and acetic acid as the most effective solvent. Unsaturated aldehydes and ketones undergo selective reduction at the carbonyl moiety in high yields in presence of $Ni\{P(OC_6H_5)_3\}_4$ as a catalyst.

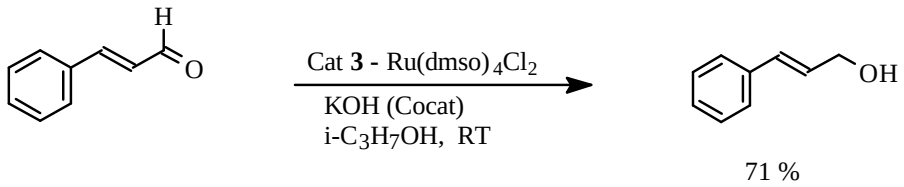
Chapter - 2

Ruthenium catalyzed transfer hydrogenation and Synthetic Applications

Novel ligands and Ru catalysts, Ru (DAB), Salen and DMSO complexes for selective transfer hydrogenation of ketones and aldehydes

Phosphines, PNNP, ethanol amines, diamines as ligands and complexes of Ru, Rh, Pd have mostly catalyze the hydrogenation of olefins.

Scheme - 2



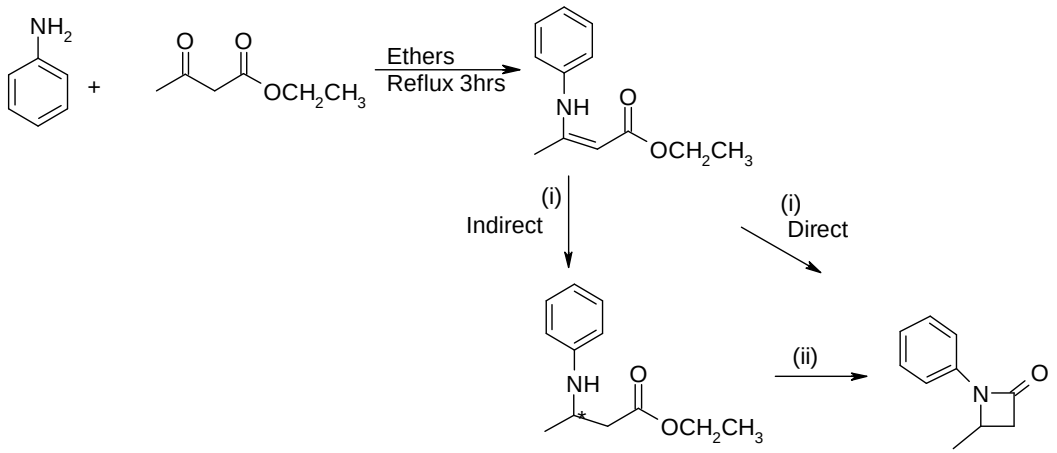
71 %

Catalyst : **1.** $Ru(DAB)_2Cl_2$ **2.** $Ru(salen)P(C_6H_5)_3Cl$ **3.** $Ru(dmso)_4Cl_2$ **4.** $Ru(dmso)_3P(C_6H_5)_3Cl_2$

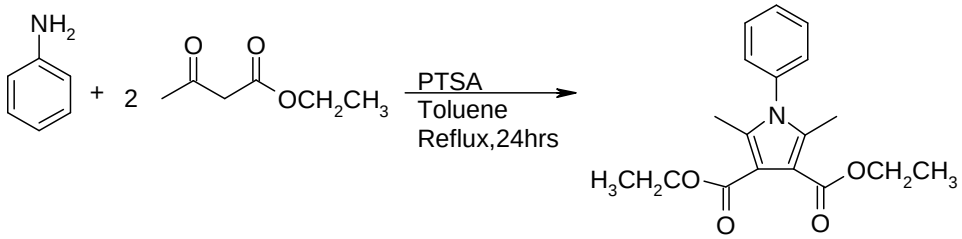
Salen, DAB and DMSO are readily available non-phosphorus ligands and excellent alternatives for the currently used phosphines ethanol amines, diamines and other ligands are used for routine transfer hydrogenation not requiring asymmetric induction. These ligands can be readily synthesized from commercially available precursors with substituents to influence the catalytic properties and asymmetric induction.

Synthetic applications

Scheme



β-Ketoester β-Lactam



β-Lactams are formed by the cyclization of the reduced β-amino esters. Both these molecules are important constituents of antibiotics and have medicinal properties.

Transfer hydrogenation of β-enamido esters will lead to the formation of β - amidoesters and intramolecular cyclization or intramolecular condensation will result in the formation of β-lactams.

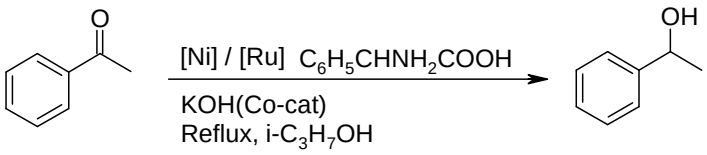
The process can be asymmetric because we start with a prochiral enamide. These enamino esters can be easily synthesized from β-keto esters and amines

Chapter - 3

Asymmetric transfer hydrogenation with racemic ligands

A fundamentally novel concept of the use of racemic ligands for asymmetric induction has been studied in these Ni and Ru complexes catalyze transfer hydrogenation reactions. Asymmetric transfer hydrogenation have been carried out using chiral ligands. Use of ethanol amines and ethylene diamines (chiral) as ligands facilitate the reduction of ketones at room temperature with high asymmetric induction.

Scheme - 3



Asymmetric transfer hydrogenation of acetophenone using (R) phenyl glycine, L-proline, threonine as chiral ligands gave low ee. Racemic phenyl glycine and phenyl

glycinol gave comparable asymmetric induction. Racemic ligands with slight excess of one enantiomer have been shown to cause high asymmetric and optical induction in the reaction of 5-pyrimidyl alkanol with a small 2 % treated with diisopropyl zinc and pyrimidine-5-carboxaldehyde. This reaction is auto catalytic, which generates more of the alkanol.

Transfer hydrogenation of β-enamido esters will lead to the formation of β -amidoesters and intramolecular cyclization or intramolecular condensation will result in the formation of β-lactams.

The process can be asymmetric because we start with a prochiral enamide. These enamino esters can be easily synthesized from β-keto esters and amines.

"When two organic fragments are found on a metal framework, the possibility of coupling them becomes an attractive prospect."

R. Hoffmann

JACS, 1982, 104, 632

CHAPTER – 1

"NICKEL CATALYZED TRANSFER HYDROGENATION"

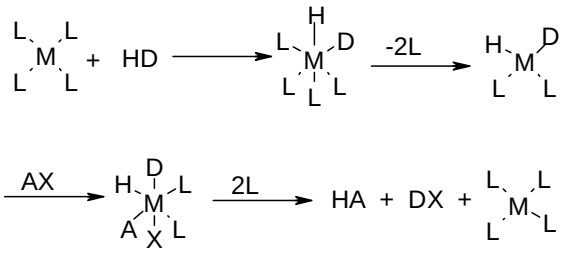
Chapter - 1

Introduction

The reduction of organic functional groups is an important reaction in organic synthesis. The transition metal catalyzed reaction has gained importance in recent years, being extremely convenient to carry out in the laboratory.[1] In comparison with catalytic reduction using molecular hydrogen, transfer reduction using hydrogen donors, has potential advantages. As molecular hydrogen, a gas of low molecular weight and, therefore, high diffusibility, it is easily ignited causing hazards on a large scale and high pressure is required for the reactions, unlike molecular hydrogen in which no pressure and simple reactions with stirring with low temperature is feasible. The reactions show enhanced selectivity with changes in catalyst adsorption, solvent and temperature.

Most of the elements suitable for catalytic homogenous reductions are part of the second transition series in the periodic tables. The complexes and salts of Pd, Pt, Ru, Ir, Rh, Fe, Ni and Co have been used as catalysts for the transfer of hydrogen from molecular hydrogen or hydrogen donors. Most active catalysts are found to be salts and complexes of Rh, Ru and Pd.

Scheme - 1



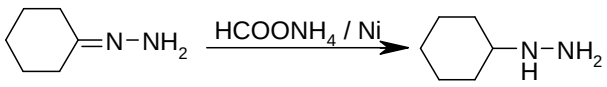
HD is a hydrogen donor (*e.g.* formic acid, in which D = CO_2H and AX is a reducible organic substrate. Oxidative additions and reductive elimination lead to the formation of a reduced species HA and regeneration of the catalyst, ML_4. The activity of the catalyst depends on the existence of free coordination sites on the central metal or producing a vacant site by loss of a ligand. For saturated complexes, the ligand-metal bond strength should be such that dissociation is possible or that ligand is displaced by solvent hydrogen donor. The mechanism depends on the nature of the catalyst, the co-ordination powers of the hydrogen donor, the hydrogen acceptor and the solvent.

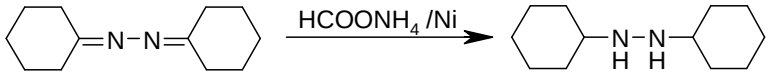
The more active hydrogen donors for homogenous catalysts are chiefly alcohols, hydroaromatics, cyclic ethers and formic acids. Despite the use of a variety of alcohols, 2-propanol remains the most popular donor, because of its simplicity, cheapness, availability and the ease of removal of both and its dehydrogenation product, acetone from reaction systems. The mechanism of hydrogen transfer from 2-propanol to a ketone substrate using $RhCl(PC_6H_5)_3$ has been extensively investigated. A synergist for this reaction is potassium hydroxide which is effective to remove a proton from the reacting complex during the part of the catalytic cycle.

More recently, the dramatic rate accelerating effect of NaOH, KOH or K_2CO_3 and other such bases, as co-catalyst in the $RuCl_2\{P(C_6H_5)_3\}_3$ catalyzed transfer hydrogenation of ketones and imines has been reported.[2] $NiCl_2$ $\{P(C_6H_5)_3\}_2$ as catalyst is also studied in the transfer hydrogenation reactions of aliphatic and aromatic aldehydes and ketones.[3] Raney Ni has been used for the transfer hydrogenation of ketones using i-propanol.[4] The disadvantage of using Raney Ni as catalyst is that is highly pyrophoric and deactivates easily, unlike transition metal catalysts, such as Ru, Os, Ir metal complexes.

We have investigated the use of $Ni\{P(OC_6H_5)_3\}_4$ as a catalyst for transfer hydrogenation using ammonium formate.[8] Ammonium formate is very versatile, selective and rapid method for catalytic hydrogenolysis. It is readily available, inexpensive, stable and non-toxic and can be used in conjunction with either palladium or carbon and Raney nickel. Moreover, it can be added to the reaction in a single portion and products can be easily separated from the reaction mixture and very convenient to use. Pd/C has now been used most often as a catalyst. Raney Ni has also been used as a catalyst for reductions of hydrazones and arenes using $HCOONH_4$

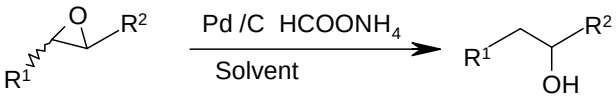
Scheme – 2





The use of Pd/C and $HCOONH_4$ as a hydrogen source is effective in the reductive ring opening of epoxides , as they are important chiral building blocks in organic synthesis and can easily undergo stereospecific ring opening reactions to form bifunctional compounds.*

Scheme – 3

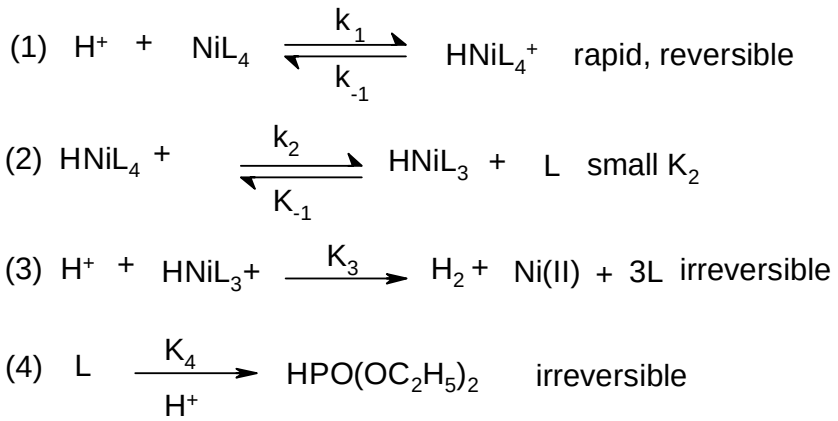


R^1= Alkyl, Aryl
R^2= H, $COOCH_3$

In 1970 it was shown that Ni (0) metal complexes are known to form NiH species in the presence of acids and are used for isomerization of olefins.

The catalyst used here is $HNi\{P(OC_2H_5)_3\}^+_4$ which is the NiH species and catalyzes the coupling of 1, 3-butadiene and ethylene to give 1,4-hexadienes, the rate limiting step is ligand dissociation from $HNiL_4^+$ to give $HNiL_3^+$ [$L=P(OC_2H_5)_3$].

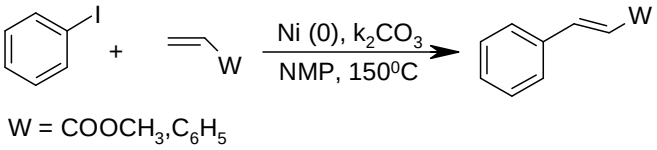
Scheme - 4



Acid used was H_2SO_4 and solvent methanol.

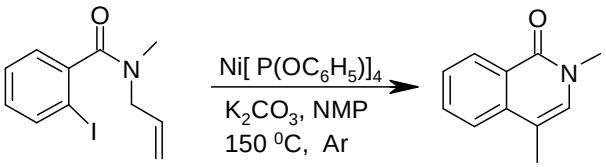
$Ni\{P(OC_6H_5)_3\}_4$ and $Ni\{P(OC_2H_5)_3]_4$ catalyze the reaction of aryl and vinyl halides with olefins (Mizoroki-Heck reaction) and alkynes is well studied. The key step in the reaction mechanism is the oxidative addition of a low valent co-ordinatively unsaturated metal complex to the aryl halide, followed by olefin co-ordination, migratory insertion and reductive elimination. These metal complexes of Ni (0) are well known to undergo ligand dissociation and have been used to catalyze the reaction of allyl acetates with nucleophiles.

Scheme – 5



In this scheme, the Mizzoroki-Heck reaction of aryliodide with styrene and ethyl acrylate in the presence of $Ni\{P(OC_6H_5)_3\}_4$ and $Ni\{P(OC_2H_5)_3\}_4$ gave high yields of the corresponding trans cinnamates and stilbenes

Scheme - 6



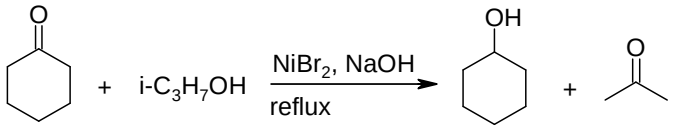
Intramolecular cyclization with 2-iodo-N-methyl allylbenzamide gave good yield 79 % of the isoquinolone as the cyclized product, while allyl-2-iodo-benzoate gave the

dehalogenated product. Homogenous catalyst like $Pd\{P(C_6H_5)_3\}_4$ has also been used for transfer hydrogenation of organic functional groups using $HCOONH_4$.*

More recently, we have reported $Ni\{P(OC_6H_5)_3\}_4$ is a better and efficient catalyst than $NiCl_2\{P(C_6H_5)_3\}_4$ which we have reported earlier*. A number of unsaturated aldehydes and ketones were reduced by $HCOONH_4$ in the presence of this Ni (0) catalyst.

The transfer hydrogenation of a range of α,β-unsaturated ketones and aldehydes using $NiBr_2$ in alkaline isopropanol.[9] Anhydrous $NiBr_2$ or $NiI_2.6H_2O$ had much higher activity than $NiCl_2.6H_2O$ in an alkaline isopropanol system. 90 % conversion of cyclohexanone was converted to cyclohexanol in 1 hr of reflux containing $NiBr_2$ as a catalyst, whereas conversions of only 14 and 24% were achieved with $NiCl_2\{P(C_6H_5)_3\}_2$ and $NiBr_2\{P(C_6H_5)_3\}_2$ under comparable conditions. A further advantage was that the system operated under aerobic conditions while the often used platinum metal, phosphine containing complexes were usually air sensitive.[10] α,β-unsaturated ketones, cyclohex-2-en-1-one, heptan-1-ol, butan-2-one, pentan-2-one, oct-1-ene, nitrobenzene and 4-nitrobenzaldehyde were reduced. Terminal olefins were reduced effectively using isopropanol but the conversion was only 27% in 0.5 hr. However, nitriles were not reduced.

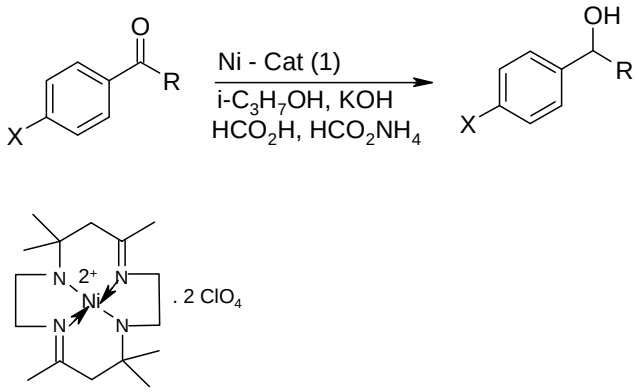
Scheme – 7



Interesting fact was that addition of 4 equivalents of $P(C_6H_5)_3$ to the $NiBr_2$ system had no effect on the rate of hydrogenation of cyclohexanone, and also $NiBr_2$ $\{P(C_6H_5)_3\}_2$ was unstable in the alkaline medium (with dissociation of phosphine).

Evidence that macrocyclic Ni (II) complex, catalyzes efficiently the chemoselective transfer reduction of carbonyl compounds in presence of propan-2-ol / KOH or HCOOH / $HCOONH_4$ as hydrogen donors to produce the alcohols in high yield.[12]

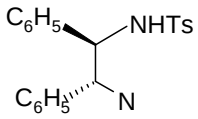
Scheme – 8



Nickel complex 1 was synthesized from literature.[13] Aliphatic aromatic carbonyl functions were reduced without affecting C=C, C-Cl, NO_2, C=N and $COOC_2H_5$ groups. A dramatic rate enhancement had been observed in the ketone reduction with excellent yield when combinations of both formic acid and ammonium formate were used

together as H-source. Alkali metal formates accelerates the rate of hydrogen transfer from formic acid in the presence of various Ru- complexes.[14] Also triethyl amine is well known to accelerate the rate of decomposition of formic acid.[15] Thus ammonium formate was activating the decomposition of formic acid, so that nickel hydride formation was facilitated which in turn, helped transfer of hydrogen to carbonyl compounds. It was observed that the reaction proceeded in excellent yield in 85% formic acid and ammonium formate.

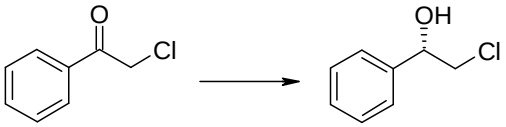
In 2001 it was illustrated that rhodium (III) versus ruthenium (II) contrasting behaviour in the asymmetric transfer hydrogenation of α-substituted acetophenones employing formic acid as the hydrogen donor. The best ligands proved to be monotosylated diamines.[16] In particular, Noyoris N-(*para*-toluene sulfonyl)-1,2-diphenylethylene diamine (TsDPEN) was possibly the optimal ligand of ruthenium (II)-catalyzed asymmetric transfer hydrogenation of ketones and imines and the rhodium (III)-catalyzed asymmetric transfer hydrogenation of imines.[17]



(R,R)- Ts DPEN

α-Tosylated acetophenone 1 was synthesized from acetophenone in two steps of yield 69% using hypervalent iodine compound (HTIB) hydroxytosyliodo benzene.[18]

Scheme - 9



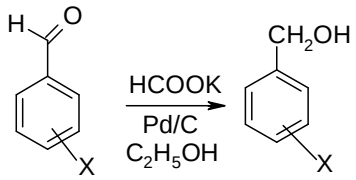
Rh 85% 75% ee

Ru 68% 85% ee

In 2003 it was reported an efficient synthesis of N-aryl Nickel (II) carbenes by protonation of Nickel (0) isocyanide complexes to exhibit transfer hydrogenation of ketones in high yield.[19]

In 2004 evidence of Pd/C-catalyzed transfer hydrogenation of benzaldehydes to benzyl alcohols using potassium formate as the selective hydrogen donor.[21]

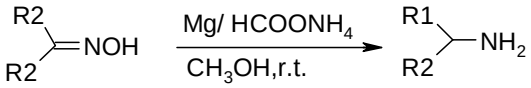
Scheme – 10



Aromatic and aliphatic aldehydes were selectively reduced to primary alcohols under mild conditions with potassium formate in the presence of Pd/C catalyst. This method is used to separate aldehydes selectively from a mixture of aldehydes and ketones. Pd-catalyst, which is heterogenous, is preferred over the transition metal catalyst like Pt, Rh and Ru.[22]

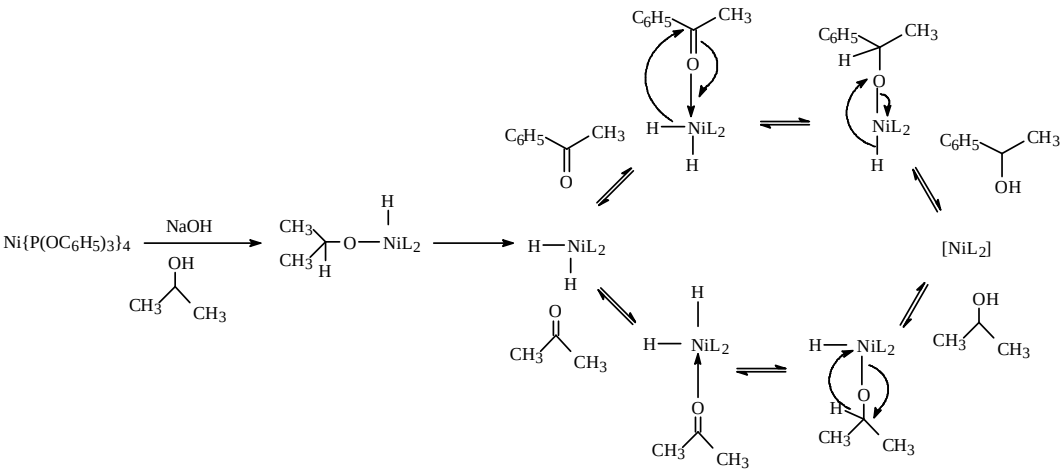
In 2004 selectively catalytic transfer hydrogenation of aldoximes and ketoximes using magnesium powder and ammonium formate at room temperature in which other

functionalities such as halogens, -OH, -OCH_3, -COOH and –CH_3 remained unaffected. The hydrogenation was fast mild, clean, cost-effective and high yielding.[23]



R_1,R_2 =H or alkyl or phenyl or sustituted phenyl group.

Fig. 1: Ni{P(OC_6H_5)$_3$}$_4$ - Ni (0) catalyzed transfer hydrogenation - catalytic cycle



The reaction proceeds *via* the following sequence (i) oxidative addition of Ni (0) to i-C_3H_7OH to form NiH species (ii) β-hydride elimination leading to acetone and a NiH_2 species (iii) coordination of the FG (Functional Group) to the NiH_2 complex and transfer of H to the coordinating FG (iv) reductive elimination of the RFG (Reduced Functional Group) by transfer of the remaining H to the co-ordinating FG and recycling of the catalyst* depicted in the Fig.1.

Objective

The aim was to use Ni (0) catalyst for the transfer hydrogenation of unsaturated aldehydes and ketones in the presence of $HCOONH_4$ and isopropanol as the transfer hydrogenating agents.

Results and Discussion

Homogenous catalyst like $Pd\{P(C_6H_5)_3\}_4$ has already been used for the transfer hydrogenation of organic functional groups using $HCOONH_4$.

Ni (0) catalyst are known to cause isomerization of olefins in presence of acids and the active species is known to be a NiH complex. Our present study involves the study of $Ni\{P(OC_6H_5)_3\}_4$ catalyst used for the oxidative addition to $HCOONH_4$ and forming NiH, which could then cause the reduction of the organic functional group.

We have found Ni (0) catalyst to be active in other transfer hydrogenation reactions where isopropyl alcohol was used as the transfer hydrogenating agent. $NiCl_2\{P(C_6H_5)_3\}_2$ has also been found to catalyze such reduction using isopropyl alcohol. Aliphatic, alicyclic and aromatic ketones undergo reduction at the carbonyl moiety in excellent yields is shown in Table.

This is the first example of a homogenous Ni (0) catalyst, which is active for the transfer hydrogenation using $HCOONH_4$ and CH_3COOH as the solvent, as the reactions proceeded at a faster rate and in high yield. The reductions of aldehydes and ketones in the presence of isopropyl alcohol as reducing agent was possible only in the presence of NaOH / KOH as a co-catalyst. Aromatic, aliphatic ketones, keto esters and aldehydes

were easily reduced to the alcohols. α,β-unsaturated aldehydes were reduced selectively to unsaturated alcohols. Aldehydes were reduced faster than ketones and the reactions were dependent on the concentration of NaOH.

The double bond in cinnamaldehyde was not reduced, which showed selective reduction at the carbonyl moiety only, thus giving cinnamyl alcohol 2-methyl cyclohexanone formed 2-methyl cyclohexanol as the product, thus giving *trans* isomers as the reduction product. Phenyl acetonitrile was not reduced with $HCOONH_4$ and isopropyl alcohol as the chief reducing agents while 4-methoxybenzylidene aniline (imine) could easily be reduced. 4-nitrotoluene was effectively reduced to 4-toluidene. Reactions were also carried out in methanol as the protic solvent, but however, the reactions were slower than isopropanol and found to be incomplete even after 24 hrs.

Thus Ni (0) catalyst was found to be the most effective and versatile catalyst for the transfer hydrogenation of aldehydes and ketones using $HCOONH_4$ as the chief reducing agent and acetic acid as the solvent. Reactions were faster and high yielding when acetic acid was used as the solvent and $HCOONH_4$ as the chief reducing agent. $Ni\{P(OC_6H_5)_3\}_4$ is the first example of a non-halide transition metal catalyst for transfer hydrogenation.

$Ni\{P(OC_6H_5)_3\}_4$ catalyst can be used for the oxidative addition to $HCOONH_4$ to for NiH species, which could then cause the reduction of the organic functional group. This Ni (0) catalyst is found to be active in other transfer hydrogenation reactions where isopropyl alcohol is used as the transfer hydrogenating agent.

This is the first example of homogenous Ni (0) catalyst being active for the catalysis of the transfer hydrogenation using $HCOONH_4$ in CH_3COOH as solvent. Reactions proceeded at a faster rate when CH_3COOH was used as a solvent than

methanol. Table-1 lists the result of our experiments. In the presence of $Ni\{P(OC_6H_5)_3\}_4$ as a catalyst, the yields were reported to be high in reducing acetophenone, cinnamaldehyde, aromatic nitro compounds, sulphonyl azide, imines which undergo reduction selectively of the carbonyl moiety. However, $C_6H_5CH_2CN$ and the double bond of ethyl cinnamate could not be reduced. Aliphatic ketones such as cyclohexanone and 2-methyl cyclohexanone were, however, reduced in 12 h. Thus aliphatic, alicyclic, aromatic aldehydes and ketones undergo readily under these conditions.

Azides were reduced readily to amines in 5 h and 97% yield. p-nitro toluene was effectively reduced to p-toluidene in 12 h. for catalytic hydrogenolysis.* Formic acid or methanol was used as the protic solvent for the reduction of azides, nitro group.

Effect of the ammonium formate and Pd/C is very versatile selective and rapid method solvent and catalysts were studied in the transfer hydrogenation of unsaturated aldehydes and ketones.

$Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of acetophenone using $HCOONH_4$ and solvent acetic acid was carried out to yield α-phenethyl alcohol in 97% yield in 5 hr, whereas $Ni\{P(OC_6H_5)_3\}_4$ catalyzed the transfer hydrogenation of acetophenone using isopropanol as the chief transfer hydrogenating agent yielded 95% of α-phenethyl alcohol in 2 hr. In this reaction, NaOH or KOH was used as the co-catalyst, the reactions were dependent on the concentration of NaOH/KOH used. Transfer hydrogenation reactions of acetophenone with $Ni\{P(OC_6H_5)_3\}_4$ as catalyst was also carried out using CH_3OH as the protic solvent but the yield was comparatively very low (68% yield) and time taken 24 hr. Thus we investigated that isopropanol was the best solvent when used in conjunction with NaOH/KOH as the co-catalyst.

$NiCl_2\{P(C_6H_5)_3\}_2$was used as a catalyst in the reduction of various aliphatic, alicyclic and aromatic ketones using isopropanol as the chief transfer hydrogenating agent and NaOH as the co-catalyst. The reductions of aldehydes proceeded at a faster rate.* Acetophenone (3 mmol) in C_3H_7OH containing $NiCl_2\{P(C_6H_5)_3\}_2$ (15 mol %) and NaOH (1 mmol) yielded phenethyl alcohol in 82% in 30 hr.

Cyclohexanone was reduced to cyclohexanol in 24 hr in 56% yield when $\{NiCl_2[P(C_6H_5)_3]_2\}$ was used as a catalyst and isopropanol as solvent and the same compound was reduced in 12 hr with 78% yield when $Ni\{P(OC_6H_5)_3\}_4$ was the catalyst acetic acid as the solvent and $HCOONH_4$ as the transfer hydrogenating agent.

Anisaldehyde was reduced in 12 hr and 76% yield when $\{NiCl_2[P(C_6H_5)_3]_2\}$ was used as a catalyst and isopropanol as the solvent. While the same was reduced in 5 hr and 80% yield when $Ni\{P(OC_6H_5)_3\}_4$ was used as a catalyst and acetic acid as the solvent and 72% yield in 8 hr when isopropanol as solvent and $Ni\{P(OC_6H_5)_3\}_4$ as the catalyst.

Cinnamaldehyde was reduced to cinnamyl alcohol in 30 hr and 51% yield when $NiCl_2\{P(C_6H_5)_3\}_2$ was used as a catalyst and isopropanol as the transfer hydrogenating agent and the same was reduced in 8 hr in 92% yield when $Ni\{P(OC_6H_5)_3\}_4$ was used as a catalyst and acetic acid as the solvent and 8 hr in 95% yield when $Ni\{P(OC_6H_5)_3\}_4$ was the catalyst and isopropanol as the solvent.

Citral was effectively reduced to geraniol with $Ni\{P(OC_6H_5)_3\}_4$ as a catalyst and isopropanol as the solvent to yield 91% of geraniol in 2 hr time.

Citronellal was reduced to citronellol in 94% yield in 16 hr when $Ni\{P(OC_6H_5)_3\}_4$ was used as the catalyst and isopropanol as the solvent.

4-Phenylbut-3-en-2-one was reduced to 4-phenyl-but-3-en-2-ol in 18 hr and 72% yield when $Ni\{P(OC_6H_5)_3\}_4$ was the catalyst and acetic acid and $HCOONH_4$ as the transfer hydrogenating agent. The same was reduced in 9 hr and 62% yield when $Ni\{P(OC_6H_5)_3\}_4$ was the catalyst and isopropanol as the hydrogenating agent.

These examples illustrate that the double bond in cinnamaldehyde, citral, citronellal and 4-phenylbut-3-en-2-one were not, however, reduced by this catalyst. The reductions are selective and undergo reductions in the carbonyl moiety only.

$Ni\{P(OC_6H_5)_3\}_4$ catalyzed the transfer hydrogenation of 4-nitrotoluene to 4-toluidine using ammonium formate and acetic acid as the solvent in 12 hr and 68% yield and the same was catalyzed in 24 hr and 59% yield when isopropanol was used as the solvent and KOH as the co-catalyst.

4-Toluene sulfonyl azide was reduced to $4\text{-}CH_3.C_6H_4.SO_2NH_2$ was reduced by $Ni\{P(OC_6H_5)_3\}_4$, $HCOONH_4$ and acetic acid as solvent in 24 hr and 97 % yield. The same was reduced in 5 hr and 88% yield when isopropanol was used as the solvent and KOH as co-catalyst.

N-Phenyl-4-methoxybenzaldimine was effectively reduced to N-phenyl-4-methoxybenzyl amine when $Ni\{P(OC_6H_5)_3\}_4$ was used as the catalyst and methanol as solvent in 20 hr and 72% yield.

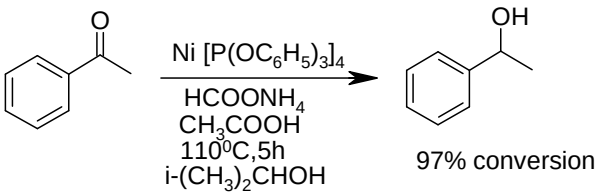
N-Phenyl-4-methoxybenzaldimine was reduced to N-phenyl-4-methoxybenzyl amine when $Ni\{P(OC_6H_5)_3\}_4$ was used as the catalyst and acetic acid as solvent with $HCOONH_4$ in 14 hr and 73 % yield.

The same was reduced in 12 hr and 75% yield when isopropanol as the transfer hydrogenating agent and KOH as co-catalyst.

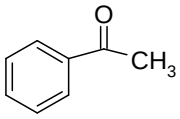
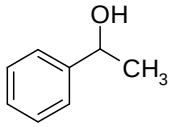
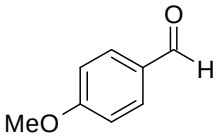
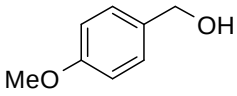
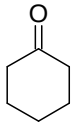
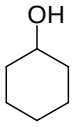
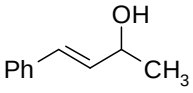
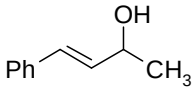
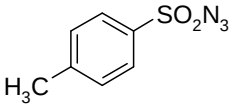
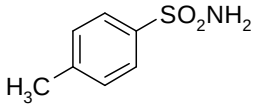
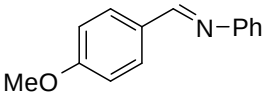
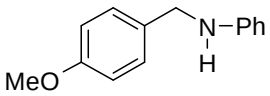
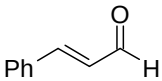
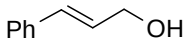
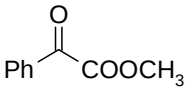
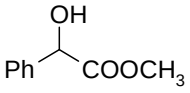
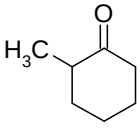
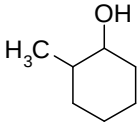
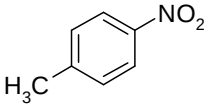
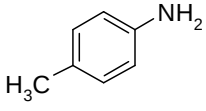
The above observations show that reactions proceeded at a faster rate when isopropanol was the solvent and KOH as co-catalyst. In the absence of co-catalyst KOH/NaOH the reaction time was 48 hr and lesser yield. Reactions were slower when methanol was used as the solvent. Reactions also gave high yield when acetic acid was the solvent and $HCOONH_4$ as the chief hydrogenating agent.

$Ni\{P(OC_6H_5)_3\}_4$ is the most effective non-halide efficient and excellent homogeneous catalyst for the transfer hydrogenation of aliphatic and aromatic unsaturated aldehydes and ketones, aromatic nitro compounds, sulphonyl azides and imines and the reduction is selective at the carbonyl moiety. However, $C_6H_5.CH_2CN$ could not be reduced.

Scheme



Table

Sr. No.	Substrate	Time, h	Product	Yield, %
1.		5		97
2.		5		80
3.		12		78
4.		18		72
5.		5		97
6.		14		73
7.		8		92
8.		8		83
9.		12		82
10.		12		68

Conclusion

$Ni\{P(OC_6H_5)_3\}_4$ is an excellent catalyst for the transfer hydrogenation of organic functional groups using ammonium formate and isopropanol as the transfer hydrogenating agents.

Experimental

General

All commercial reagents were obtained from Aldrich Chemical Co., S.D. Fine Chemical Co. India, and LOBA Chemical Co., India. Progress of the reaction was monitored by TLC and visualized by UV absorption by fluorescence quenching by I_2 staining or by both. Silica gel 60-120 and 100-200 mesh obtained from S.D. Fine Chemical Co., India, and Rico Industrial Chemicals Co., India, for column chromatography. All melting points were uncorrected in Degree Celsius and recorded on a Thermonik Melting Point apparatus.

IR spectra were recorded on a Perkin-Elmer Infrared Spectrometer model 599-B and model 1620 FT-IR. ^{1}H-NMR spectra were recorded using TMS as internal reference on Bruker AC-200, Bruker MSL-300 and Bruker-500 instruments using $CDCl_3$ as solvent chemical shifts are reported in δ. Mass spectra were recorded on Finnigan-Mat 1020C mass spectrometer and are obtained at an ionization potential of 70 Ev.

Preparation of catalyst

A mixture of nickel nitrate (0.76 g, 4.4 mmol) and triphenyl phosphite (3.9 g, 13 mmol) in ethanol (10 ml) was charged into a 50 ml conical flask. To this stirred solution, sodium borohydride (0.25 g, 6.94 mmol) in warm ethanol (10 ml) was added slowly for 10 minutes. The white precipitate obtained was filtered, washed with ethanol and dried. m.p. 145°C.

Experimental

1. $\{Ni[P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of acetophenone using $HCOONH_4$

A solution of acetophenone (0.239 g, 2 mmol), ammonium formate (0.63 g, 10 mmol) and $Ni\{P(OC_6H_5)_3\}_4$ (0.13 g, 0.1 mmol) in CH_3COOH (10 ml) was refluxed for 5 hr. The progress of the reaction was monitored by TLC. After the reaction was complete, the solvent was removed on rotavap and the residue extracted into ethyl acetate, washed with saturated $NaHCO_3$, brine, dried over anhydrous Na_2SO_4 and concentrated and purified by column chromatography over silica gel to give α-phenethyl alcohol in 0.359 g (97% yield).

B.P. : 83-84°C / 9mm of Hg

IR (cm^{-1}) 3320, 2980, 2940, 2900, 2800, 2460, 1960, 1895, 1615, 1505, 1460, 1380, 1225, 1070, 1020, 910, 750.

^{1}H-NMR (δ, $CDCl_3$, 80 MHz): 7.23 (m, 5H, Ar), 4.83-4.5 (q, 8Hz, 1H, CH.CH_3), 4.0 (s, 1H, OH), 1.3-1.2 (d, 8Hz, 3H, CH.CH_3).

2. Ni{P(OC_6H_5)$_3$}$_4$ catalyzed selective transfer hydrogenation of cinnamaldehyde using $HCOONH_4$

A solution of cinnamaldehyde (0.264 g, 2 mmol), ammonium formate (0.63 g, 10 mmol) and Ni{P(OC_6H_5)$_3$}$_4$ (0.13 g, 0.1 mmol) in CH_3COOH (10 ml) was refluxed for 8 hr. The progress of the reaction was monitored by TLC. After the reaction was complete, the solvent was removed on rotavap and the residue extracted into ethylacetate, washed with saturated anhydrous $NaHCO_3$, brine, dried over Na_2SO_4 and concentrated and purified by column chromatography over silica gel to give cinnamyl alcohol 0.370 g (92% yield).

B.P.: 250°C.

IR (cm^{-1}): 3450, 3010, 2850, 1600, 1500, 1450, 1200, 1085, 1060, 1010, 960, 740, 690.

^{1}H-NMR (δ, $CDCl_3$, 80 MHz): 7.2 (m, 5H, Ar), 6.8-6.11 (m, 2H, CH=CH), 4.23 (d, 2H, CH_2), 1.68 (bs, 1H, OH).

3. Ni{P(OC_6H_5)$_3$}$_4$ catalyzed transfer hydrogenation of 4-phenylbut-3-en-2-one using ammonium formate

A solution of 4-phenylbut-3-en-2-one (0.291 g, 2 mmol), ammonium formate (0.63 g, 10 mmol) and Ni{P(OC_6H_5)$_3$}$_4$ (0.13 g, 0.1 mmol) in CH_3COOH (10 ml) was refluxed for 18 hr. The reaction mixture was monitored by TLC and after the reaction

was complete, the solvent was removed on rotavap and the residue extracted into ethyl acetate, washed with saturated anhydrous $NaHCO_3$, brine, dried over Na_2SO_4 and concentrated and purified by column chromatography over silica gel to give 4-phenyl-but-3-en-2-ol (0.359 g, 72%) yield.

IR (cm^{-1}): 3310, 3010, 2985, 1450, 1370, 1140, 1060, 760, 700, 540, 390.

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 7.5-7.25 (m, 5H, Ar), 6.64-6.57 (d, 14Hz, 1H, C_6H_5 CH=), 6.34-6.24 (dd, 14, 6Hz, 1H, =CH.CHOH), 4.6-4.45 (m, 1H, CH.OH), 1.9 (bs, 1H, OH), 1.42-1.39 (d, 6Hz, 3H, CH.CH_3)

4. Ni{P(OC_6H_5)$_3$}$_4$ catalyzed transfer hydrogenation of 4-toluene sulfonyl azide using ammonium formate

A solution of 4-toluenesulfonylazide (0.367 g, 2 mmol), ammonium formate (0.63 g, 10 mmol) and Ni{P(OC_6H_5)$_3$}$_4$ (0.13 g, 0.1 mmol) in CH_3COOH (10 ml) was refluxed for 5 hr. The progress of the reaction was monitored by TLC. After the reaction was complete, the solvent was removed on rotavap and the residue was extracted with ethyl acetate, washed with saturated $NaHCO_3$, brine, dried over anhydrous Na_2SO_4 and concentrated and purified by column chromatography over silica gel to give a mixture of 4-$CH_3C_6H_4SO_2NH_2$ (Yield : 0.500 g, 97%).

IR (cm^{-1}): 3310, 3240, 2960, 2920, 2860, 1580, 1460, 1380, 1330, 1160, 1100, 910, 820, 710, 680.

^{1}H-NMR: 7.12-7.07 (d, 10 Hz, 2H, C_6H_4), 6.23 (bs, 2H, NH_2), 2.25 (s, 3H, CH_3).

5. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of 4-nitrotoluene using ammonium formate

A solution of 4-nitrotoluene (0.237 g, 2 mmol), ammonium formate (0.63 g, 10 mmol) and $Ni\{P(OC_6H_5)_3\}_4$ (0.13 g, 0.1 mmol) in CH_3COOH (10 ml) was refluxed for 12 hr. The reaction mixture was monitored by TLC and after completion, concentrated on rotavap, neutralized with $NaHCO_3$ (saturated), extracted with ethyl acetate. The combined organic extracts washed with water, brine and dried over anhydrous Na_2SO_4, concentrated to give a mixture of 4-toluidene (0.220 g, 68.5%).

IR (cm^{-1}): 3300, 3200, 2800, 2820, 1610, 1500, 1450, 1370, 1180, 1110, 1030, 810, 500.

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 7.07-7.01 (d, 12 Hz, 2H, $C_6\underline{H}_4$), 6.68- 6.62 (d, 12 Hz, 2H, $C_6\underline{H}_4$), 3.60 (bs, 2H, $N\underline{H}_2$), 2.32 (s, 3H, CH_3)

6. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of benzoin using ammonium formate

A solution of benzoin (0.636 g, 3 mmol), ammonium formate (1.513 g, 24 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.1 g, 0.077 mmol) was refluxed in acetic acid (10 ml) for 5 hr. The reaction mixture was monitored by TLC and after completion, concentrated on a rotary evaporator, neutralized with saturated $NaHCO_3$, extracted with ethylacetate, the combined organic extracts washed with water, brine, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography over silica gel (100-200 mesh) to give diphenyl ethylene glycol (0.497 g, 72%).

IR (cm^{-1}): 3300, 1450, 1380, 1020, 700, 500, 370.

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 7.4-7.1 (m, 10H, Ar), 4.85 (s, 2H, $C_6H_5.CH$), 4.72 (s, 2H, $C_6H_5.CH$), 2.95 (bs, 2H, CH.OH minor), 2.32 (bs, 2H, CH.OH major).

7. Ni{P(OC_6H_5)$_3$}$_4$ catalyzed transfer hydrogenation of N-phenyl-4-methoxy benzaldimine using ammonium formate

A solution of N-phenyl-4-methoxybenzaldimine (0.422 g, 2 mmol), ammonium formate (1.513 g, 24 mmol), Ni{P(OC_6H_5)$_3$}$_4$ (0.1 g, 0.077 mmol) was refluxed in methanol (10 mL) for 20 hr. The reaction mixture was monitored by TLC and after completion, concentrated on a rotary evaporatory, neutralized with saturated $NaHCO_3$, extracted with ethyl acetate, the combined organic extracts washed with water, brine, dried over anhydrous Na_2SO_4 concentrated to give a mixture of N-phenyl-4-methoxybenzyl amine (0.308 g, 73%).

IR (cm^{-1}): 3300, 1590, 1490, 1450, 1230, 1160, 1010, 750, 690, 530;

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 8.5 (s, 1H, NH), 7.45-7.01 (m, 7H, Ar), 6.85-6.77 (d, 16Hz, 2H, C_6H_4), 4.92 (s, 2H, CH_2), 3.72 (s, 3H, OCH_3).

8. Ni{P(OC_6H_5)$_3$}$_4$ catalyzed transfer hydrogenation of citral using isopropyl alcohol

A solution of citral (0.304 g, 2 mmol), Ni{P(OC_6H_5)$_3$}$_4$ (0.1 g, 0.077 mmol), KOH (0.02 g, 0.36 mmol), was refluxed in isopropyl alcohol (10 mL) for 2 hr and

monitored by TLC. After completion, the reaction mixture was concentrated on a rotary evaporator, extracted with ethyl acetate and washed with 10% HCl (3 x 25 ml), brine, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography over silica gel to give geraniol (0.280 g, 91%).

IR (cm^{-1}): 3300, 2800, 1430, 1370, 1050, 1000;

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 5.45-5.32 (t, 6Hz, 1H, C=C<u>H</u>.CH_2), 5.15-5.05 (t, 6Hz, 2H, C=<u>CH</u>.CH_2), 4.16-4.13 (d, 6Hz, 2H, <u>Ch</u>$_2$.OH), 1.60 (s, 6H, C=(C<u>H</u>$_3$)$_2$), 1.50-1.05 (m, 4H, CH.C<u>H</u>$_2$.C<u>H</u>$_2$.C=), 0.90-0.87 (s, 6Hz, 3H, C.<u>CH</u>$_3$).

9. Ni{P(OC_6H_5)$_3$}$_4$ catalyzed transfer hydrogenation of citronellal using isopropyl alcohol

A solution of citronellal (0.304 g, 2 mmol), Ni{P(OC_6H_5)$_3$}$_4$ (0.1 g, 0.077 mmol), KOH (0.02 g, 0.36 mmol) was refluxed in isopropyl alcohol (10 mL) for 16 hr and monitored by TLC. After completion, the reaction mixture was concentrated on a rotary evaporator, extracted with ethyl acetate and washed with 10% HCl (3 x 25 ml), brine, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography over silica gel to give citronellal (0.294 g, 94%).

IR (cm^{-1}): 3200, 2800, 1650, 1390, 1320, 1000, 450.

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 5.15-5.05 (m, 1H, C=<u>CH</u>.CH_2), 3.72-3.60 (m, 2H, C<u>H</u>$_2$OH), 2 (m, 2H, <u>CH</u>$_2$), 1.68 (s, 3H, <u>CH</u>$_3$), 1.58 (s, 3H, <u>CH</u>$_3$), 1.40-1.1 (m, 4H, C.<u>Ch</u>$_2$.<u>CH</u>$_2$.C), 0.9-0.8 (m, 4H, =C.<u>CH</u>$_3$) and C<u>H</u>(CH_3)$_2$.

10. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of cyclohexanone using ammonium formate

A solution of cyclohexanone (2.94 g, 3 mmol), ammonium formate (1.513 g, 24 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.1 g, 0.077 mmol) was refluxed in acetic acid (10 mL) for 12 hr. The reaction mixture was monitored by TLC and after completion, concentrated on a rotary evaporator, neutralized with saturated $NaHCO_3$, extracted with ethylacetate. The combined organic extracts washed with water, brine, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography over silica gel (100 - 200 mesh) to give cyclohexanol (2.34 g, 78%).

IR (cm^{-1}): 3300, 2900, 2850, 1450, 1300, 1100, 1000, 1050

^{1}H-NMR (δ, $CDCl_3$, 80 MHz): 3.5 (m, 1H, O<u>H</u>), 0.9-2.3 (m, OH, 10H, C<u>H</u>$_2$).

11. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of 2-methyl cyclohexanone using ammonium formate

A solution of 2-methyl cyclohexanone (0.336 g, 3 mmol), ammonium formate (1.513 g, 24 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.1 g, 0.077 mmol) was refluxed in acetic acid (10 mL) for 12 hr. The reaction mixture was monitored by TLC and after completion, concentrated on a rotary evaporator, neutralized with saturated $NaHCO_3$, extracted with ethyl acetate, the combined organic extracts washed with water, brine, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography over silica gel (100 - 200 mesh) to give 2-methylcyclohexanol (0.270 g, 82%).

IR (cm^{-1}): 3300, 2850, 1490, 1335, 1350, 1280, 1125, 1050, 970

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 3.5 (m, 1H, OH), 0.9-2.5 (m, 12H, $C\underline{H}_3C\underline{H}_2C\underline{H}$-).

12. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of phenylacetonitrile

A solution of phenyl acetonitrile (0.351g, 3 mmol) ammonium formate (1.513 g, 24 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.1 g, 0.077 mmol) was refluxed in acetic acid (10 mL) for 24 hr. The reaction mixture was monitored by TLC. However, even after 24 hr of reflux TLC remain unchanged and there was no formation of 2-phenylethylamine.

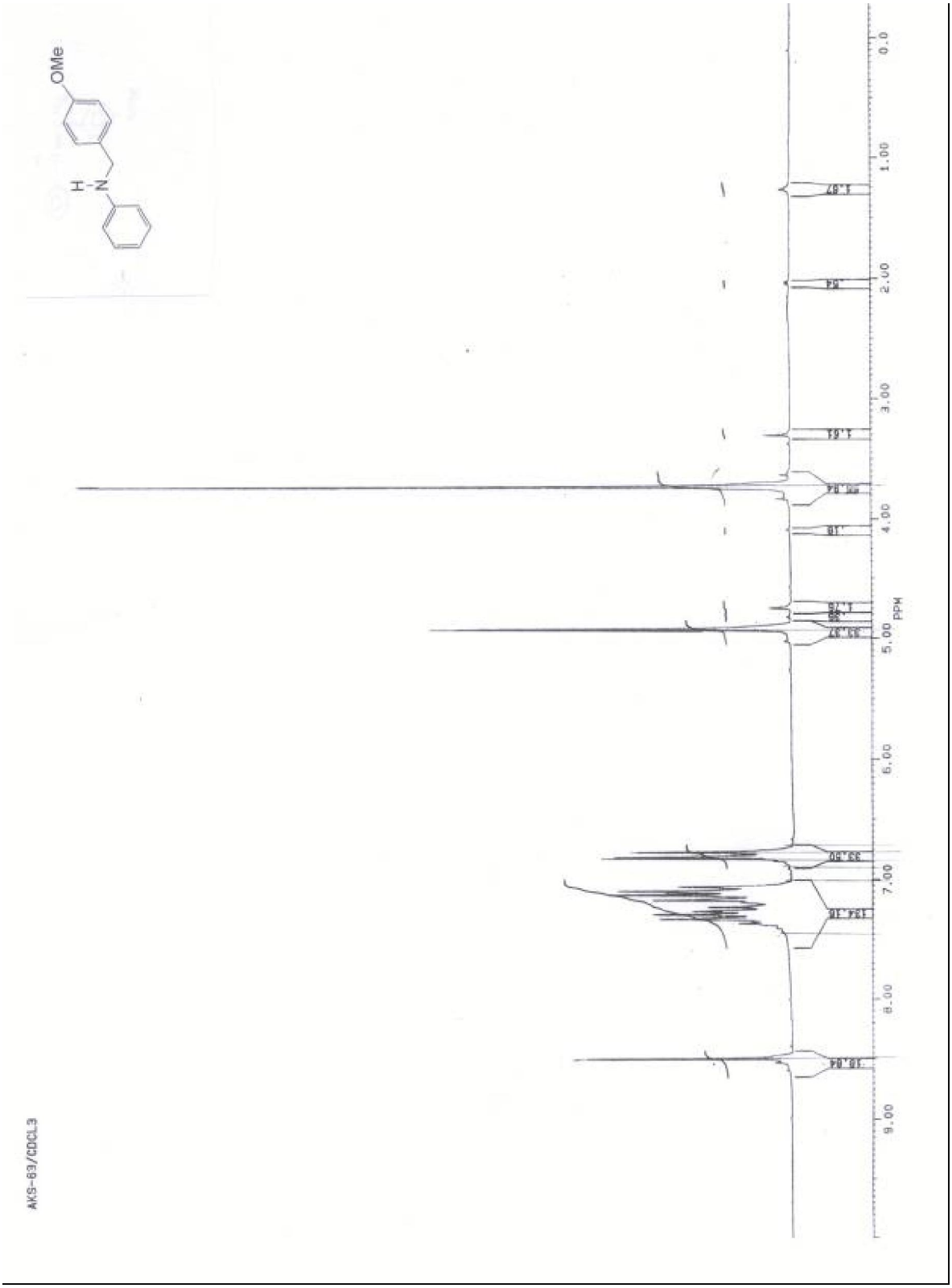
13. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of benzoylmethylformate using ammonium formate

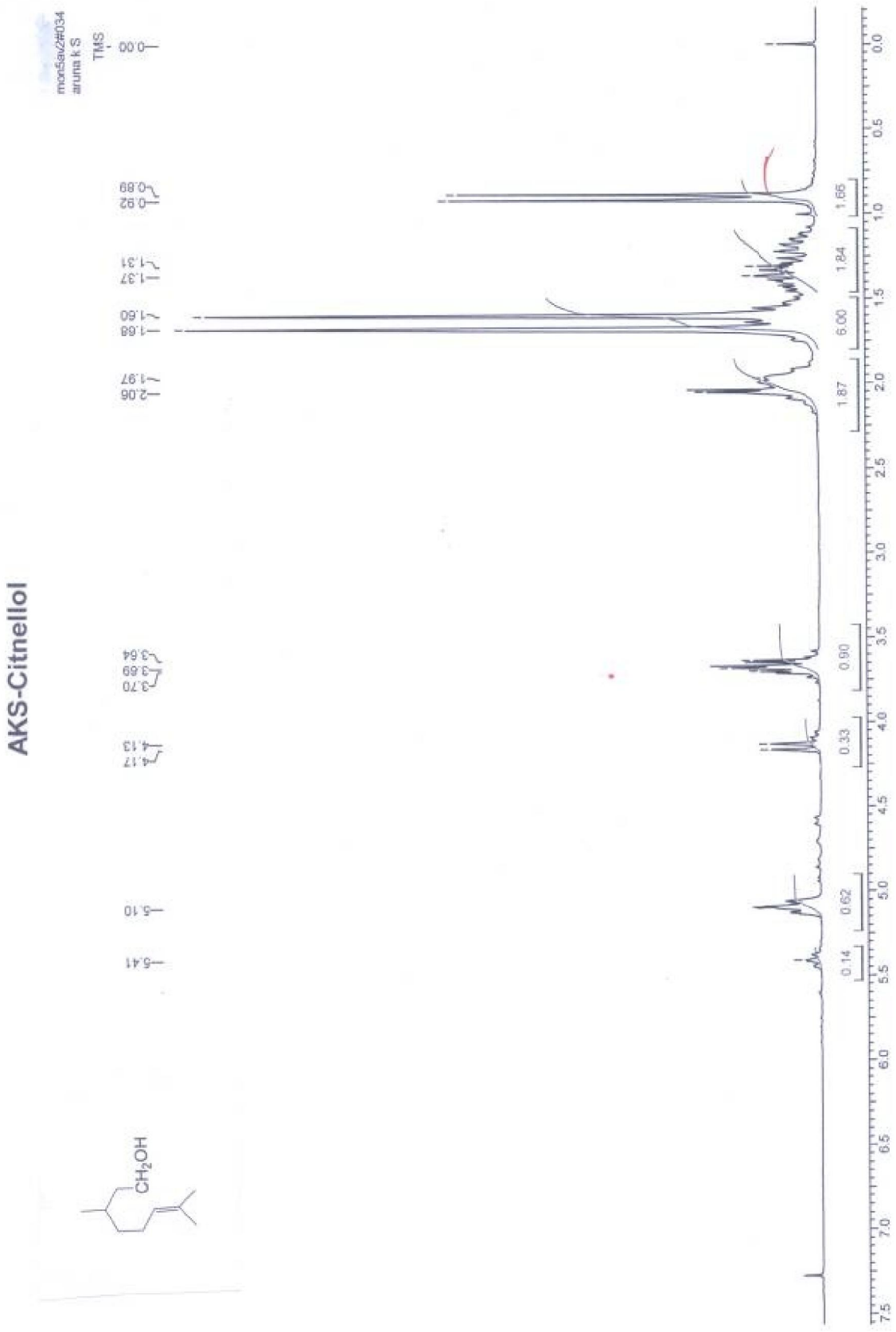
A solution of benzoylmethylformate (0.492 g, 3 mmol), ammonium formate (1.513 g, 24 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.1 g, 0.077 mmol) was refluxed in acetic acid (10 ml) for 8 hr. The reaction mixture was monitored by TLC and after completion, concentrated on rotary evaporator, neutralized with saturated $NaHCO_3$, extracted with ethyl acetate; the combined organic extracts washed with water, brine, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography over silica gel (100 - 200 mesh) to give methyl mandelate (0.284 g, 83%).

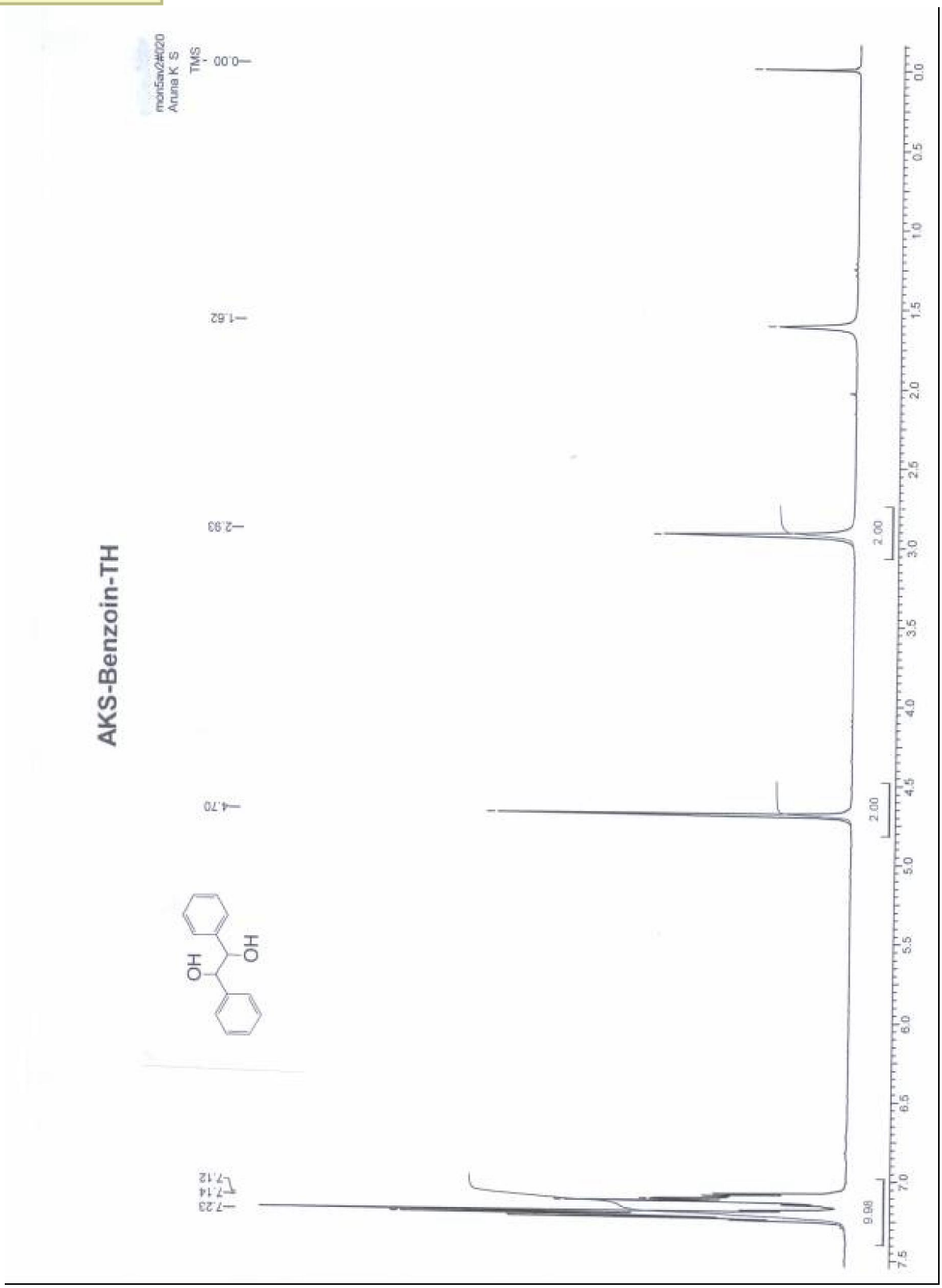
B.P. 135°C/12mm of Hg

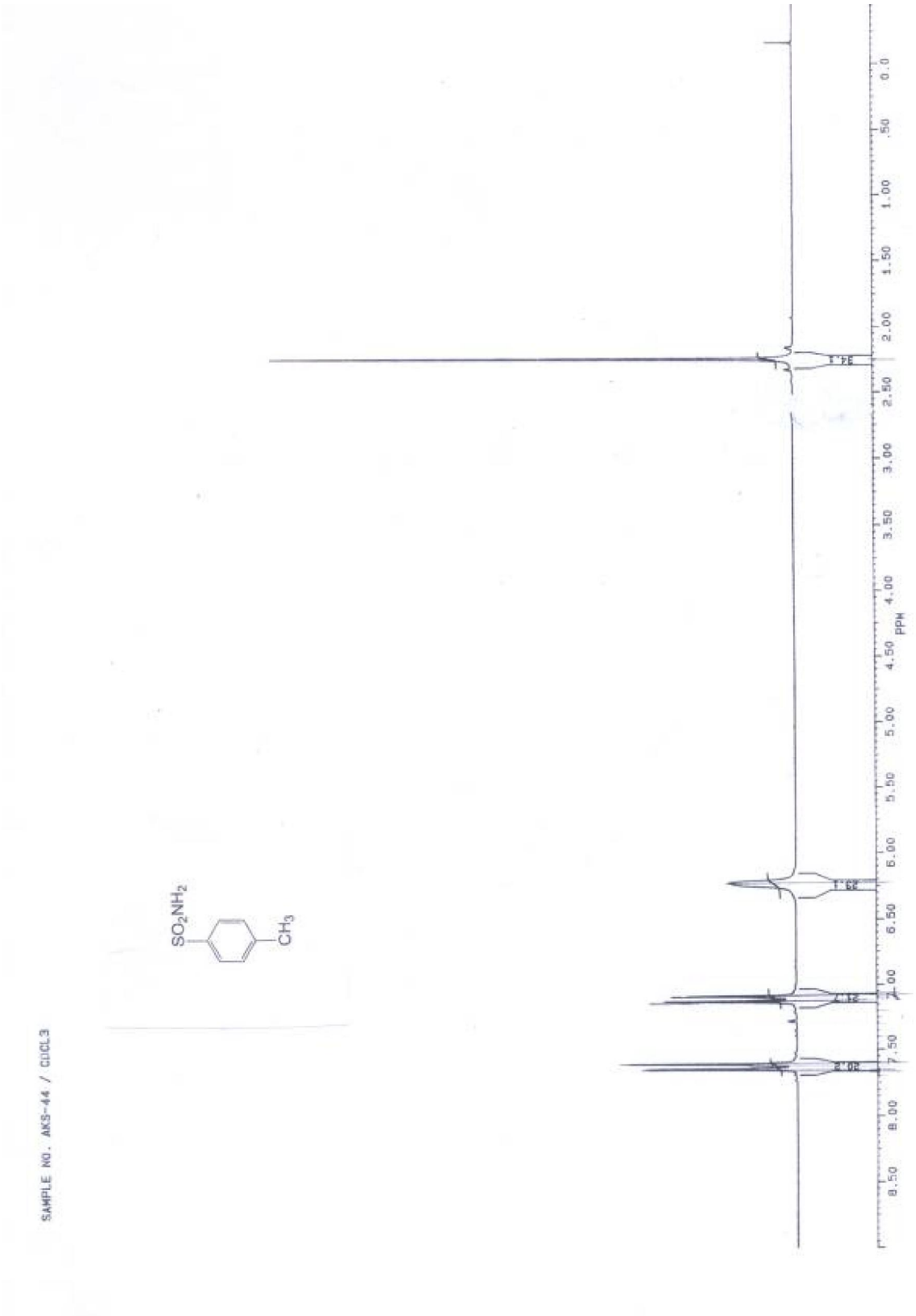
IR (cm^{-1}): 3520, 3030, 2970, 1745, 1610, 1505, 1450, 1300, 1230, 1100, 1080, 760, 680

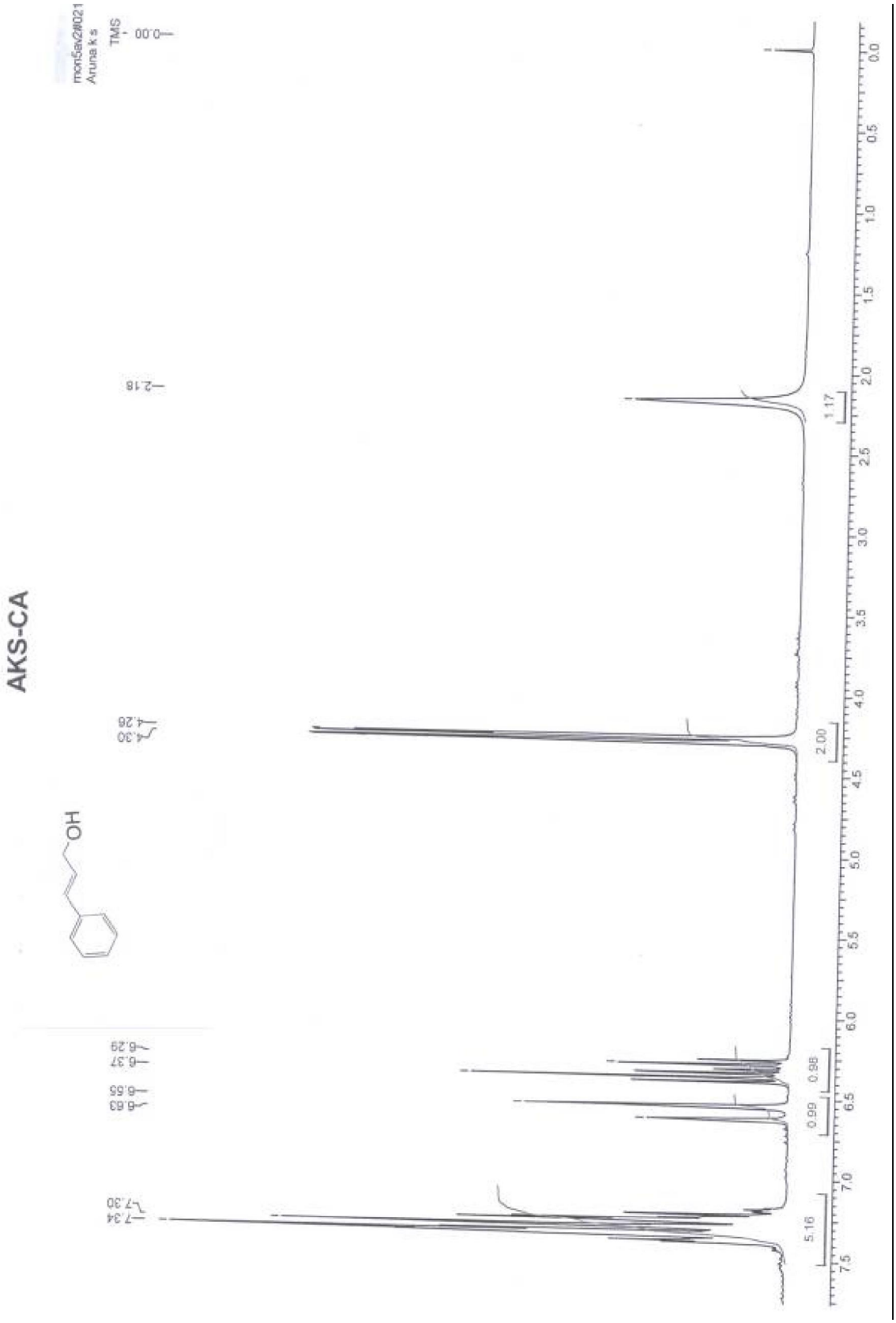
^{1}H-NMR (δ, $CDCl_3$, 90 MHz): 7.29 (bs, 5H, Ar), 5.13 (d, 1H, $C_6H_5.C\underline{H}$), 3.69 (s, 3H, $COOC\underline{H}_3$), 3.42 (d, 1H, O<u>H</u>).

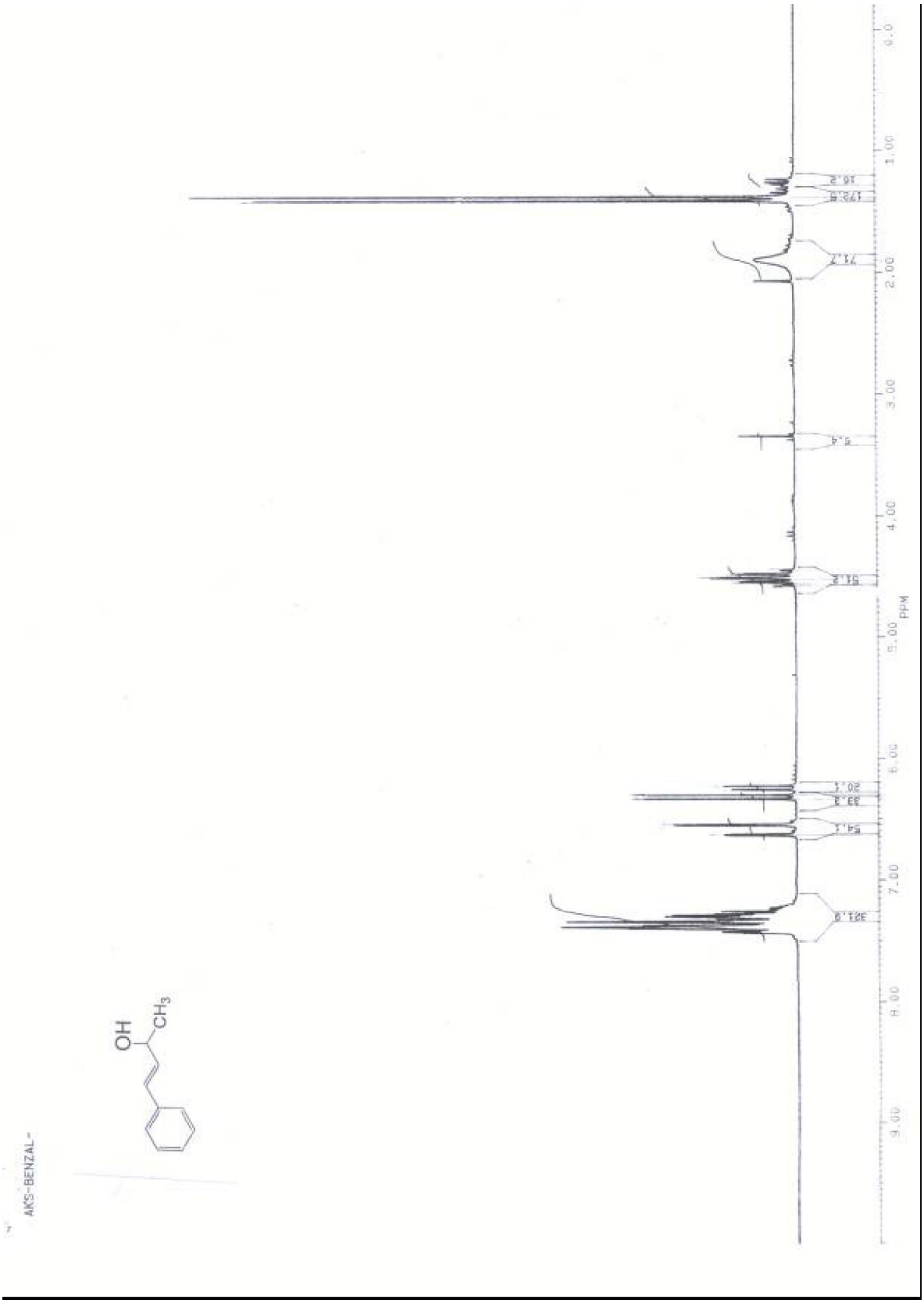












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Chapter - 2

Introduction

Catalytic transfer hydrogenation using Ru, Rh and Ir complexes has gained tremendous importance in the laboratory for reduction of various functional groups. The ability of ruthenium complexes to dehydrogenate alcohols and deliver the hydrides to a α, β - unsaturated ketone in the transfer hydrogenation.

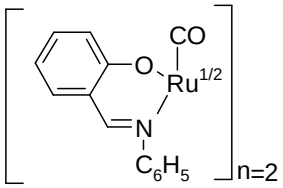
In 1988 it was reported that a base is required in the RuH_2 (N_2) $(PC_6H_5)_3$ catalyzed thermal production of hydrogen from different alcoholic substrates. The role of the base is to generate a nucleophilic alkoxide ion which is to generate a nucleophilic alkoxide ion which is to generate a nucleophilic alkoxide ion which would rapidly attack the Ru complex for dehydrogenation.

The effect of base like NaOH on $RuCl_2(P(C_6H_5)_3)_3$ was studied for various ketones using refluxing isopropanol as the solvent.

Salen and DMSO complexes of Ru, Rh, Pd have been widely used for the hydrogenation of olefins..

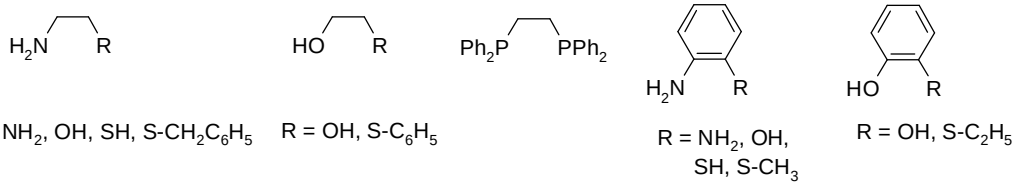
In 1978 new salicyl aldimine chelates of divalent and trivalent ruthenium from $RuCl_2$ $(PPh_3)_3$ were synthesized. The Ru (II) complex trans Ru(Salen) $(PPh_3)_2$ is stable in solid form, but very unstable to oxidation in solution. Ru-(III) derivative, Ru (Salen), Cl (PPh_3) displays magnetic properties.

Calderazzo *et al*. in 1969 reported the synthesis of carbonyl [N, N'-ethylene bis (salicylaldiminato) (2-)] ruthenium and dicarbonyl (N-phenyl salicylaldiminato) ruthenium by heating the free ligands with $Ru_3(CO)_{12}$



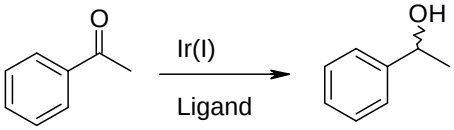
Co Salen supported on zeolite and amino-sulphoxide Ir complexes have been used for the reduction of ketones. Both formic acid and 2-propanol proved to be suitable hydrogen donors.

In 2000 asymmetric transfer hydrogenation of acetophenone using Ir (I) ligand with simple amino sulfoxides as ligands were synthesized with high enantioselectivity.



R = NH_2, OH, SH, S-$CH_2C_6H_5$ R = OH, S-C_6H_5 R = NH_2, OH, SH, S-CH_3 R = OH, S-C_2H_5

Scheme –1

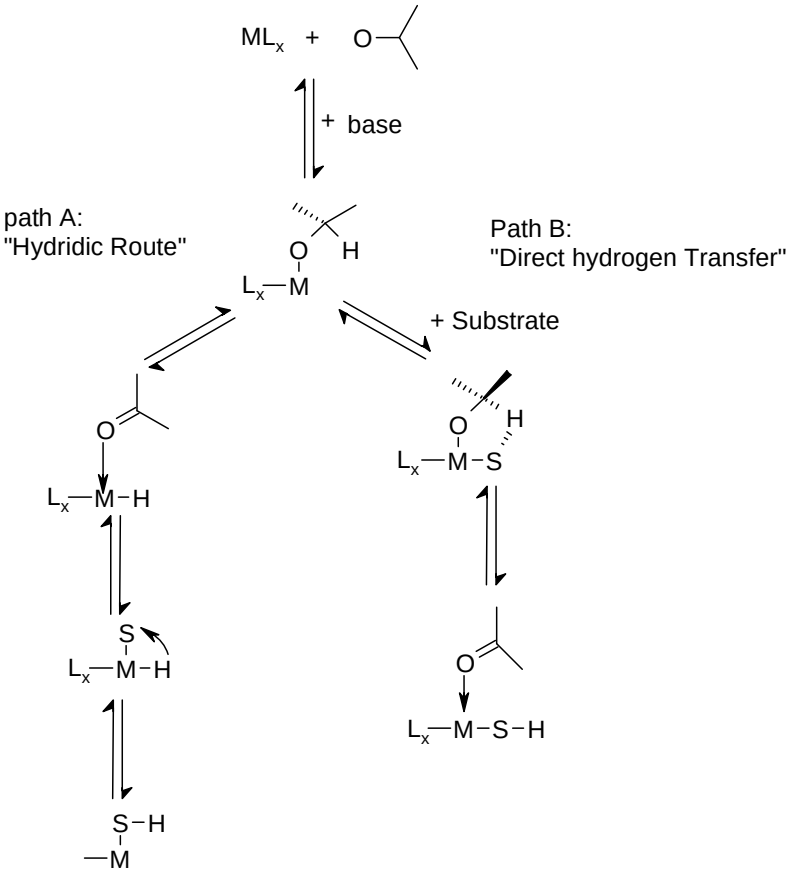


From a mechanistic point of view, two general pathways can be envisaged for transfer hydrogen as in (*Fig*. 1) a stepwise process through a hydride complex (path A) and a concerted process in which the hydrogen is directly transferred from the hydrogen donor to the substrate (“direct hydrogen transfer” path B).

Noyori and co-workers in 1997 showed that structure of the supposed active species in ruthenium II-catalyzed transfer hydrogenation is a ruthenium II 16-electron

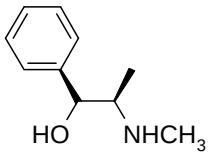
complex. In the presence of 2-propanol, an 18-electron ruthenium hydride species is formed that catalyzes the reduction of various ketones.

Figure 1.

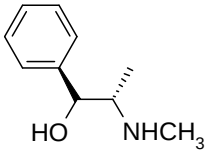


Asymmetric transfer hydrogenation of aromatic ketones in 2-propanol was carried out by using the iridium (I) complexes prepared from [Ir Cl (COD)]$_2$ and a variety of chiral diamine ligands, derived from α-amino acids. Good catalytic activity and enantioselectivity were observed in the presence of KOH at room temperature.

Noyori *et al*. in 1996 showed that enantioselectivity of the reaction using Ru(II) complexes with chiral nitrogen ligands, such as 1,2-diphenyl-ethylene diamine derivatives and β-amino alcohol derivatives was very high.



(1S,2R)



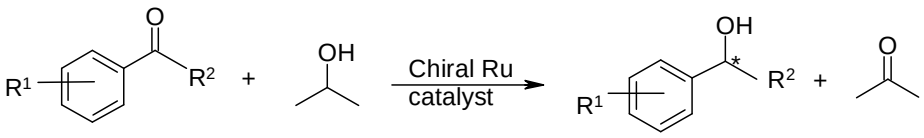
(1S,2S)

Asymmetric transfer hydrogenations of ketones in 2-propanol

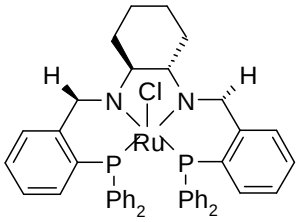
2-Propanol is the conventional hydrogen source having favourable properties as it is stable, easy to handle (b.p. 82°C) non-toxic, environment friendly and inexpensive and dissolves many organic compounds. The acetone product is easily removable Ru-complexes are well shaped having C_2-chiral ligands.

Thus asymmetric catalytic transfer hydrogenation of acetophenone derivatives proceeds at room temperature using a tetradentate diphosphine or diamine ligand or a diphosphine or diimine ligand with 2-propanol as the solvent and $(CH_3)_2CO^-K^+$ as co-catalyst.

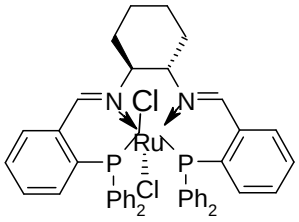
Scheme - 2



Chiral ligands of Ruthenium



(S,S) -1



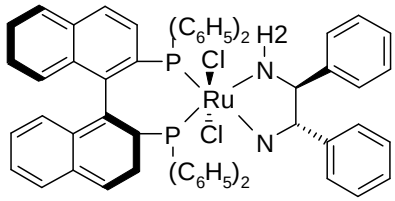
(S,S) -2

Various substituted 1-phenyl ethanols were obtained in high yields with 97% ee. The rate and enantioselectivity were sensitive to the steric crowding of the substrates as well as the electronic properties of the ring substituents.

Salen, DAB and DMSO are readily available non-phosphorous ligands and are excellent alternatives for currently used phosphines, ethanol amines, diamines and ether ligands, for routine transfer hydrogenations not requiring asymmetric induction.

In 2001 asymmetric transfer hydrogenation of simple ketones[13] in isopropyl alcohol was done by using trans $RuCl_2$ [(S)-binap] [(S,S)dpen] 1 (binap = (1,1'-binaphthalene-2,2'-diylbis (diphenyl-phosphane] : dpen = diphenylethylenediamine). The enantiomeric excess was upto 99%, high chemoselectivity for carbonyl over olefin reduction.[14]

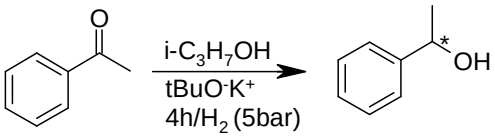
Ligand 1



trans- $RuCl_2$ [(S) - BINAP] [(S,S) - DEPN]

(1)

Scheme – 3



Catalytic hydrogenation with 1 shows that the catalyst requires the presence of alkali metal cations.

Evidence of the use of amino amides derived from proline as chiral ligands in the ruthenium (II)-catalyzed transfer hydrogenation reaction of ketones gave enantioselectivity of 98.8%, in which isopropanol is the hydrogen source.

In 2001, reactivity of (n^4-tetraphenyl cyclopentadienone) (CO_2) Ru ($HOCH(CH_3)_2$) found unexpected stability of the neutral 2-propanol - Ruthenium (0) complex with respect to β-hydride elimination.[17]

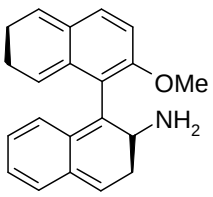
A novel Ruthenium-acetamido complex synthesized from the reaction of $[P(Cy_3)_2$ (CO) $(CH_3CN)_2$ $RuH]^+BF_4$ with KOH in 2-propanol and was found to be an effective catalyst for the transfer hydrogenation of carbonyl compounds and imines which provided a stepwise mechanism of proton and hydride transfer *via* a coordinately unsaturated ruthenium-amido species.[18]

In 2002 evidence of a practical synthesis of optically active amino alcohols *via* asymmetric transfer hydrogenation of functionalized aromatic ketones.[19] 2-substituted acetophenones such as 2-cyano-2-azido-, or 2-nitroacetophenones were effectively reduced with a mixture of HCOOH / $N(C_2H_5)_3$ containing a chiral Ru(II) catalyst, RuCl [(S,S)-N-(*p*-toluenesulfonyl)-1,2-diphenyl ethylene diamine) (*p*-cymene), giving the corresponding optically active alcohols, which can be converted to optically active amino alcohols with excellent ee's.

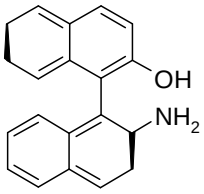
In 2002, it was reported that catalytic activity of ruthenium complexes of terdentate phosphorus-nitrogen-phosphorus (PNP) and bidentate phosphorus-nitrogen (PNH) ligands for the catalytic transfer hydrogenation for the reduction of ketones to alcohols using isopropanol to get high enantioselectivity upto 87%.[20]

In 2002, high enantioselectivity in the transfer hydrogenation of acetophenone with 2-propanol using Ru complexes of the schiff base derived from (S)-2-amino-2'-hydroxy-1,1-binaphthyl (NOBIN) and 2-pyridenecarbaldehyde which afforded (S)-1-phenylethanol in nearly quantitative yields and outstanding selectivities of upto 97% ee.[22]

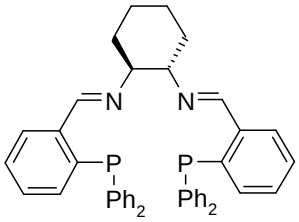
Ligands :



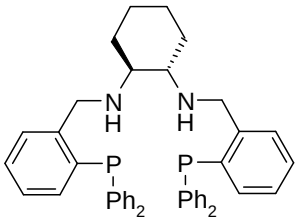
(S)-NOMBIN



(S)-NOBIN



(1)
$R = C_6P_2N_2$

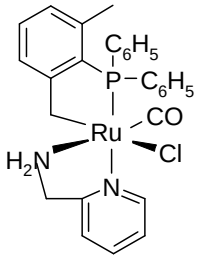


(2)
$R = C_6P_2(NH)_2$

Ligand 2 exhibited remarkable catalytic activity and 99% enantioselectivity under ambient conditions, with $[IrHCl_2(COD)]_2$ catalyst.

In 2004, cyclometalated Ruthenium (II) complexes were synthesized as highly active transfer hydrogenation catalysts.[25]

Catalyst 1 :



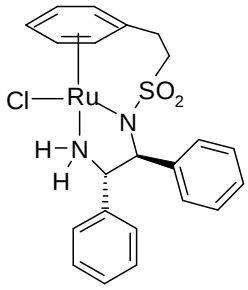
A large number of alkyl, aryl, dialkyl (linear and cyclic) and diaryl ketones were converted to alcohols within a few minutes using catalyst 1. Ketones containing an olefinic function (5-hexen-2-one) could be selectively converted into the corresponding alcohol without hydrogenation or isomerization of the double bond

In 2004, the importance of 1,2, anti-disubstitution in monotosylated diamine ligands for ruthenium (II)-catalyzed asymmetric transfer hydrogenation was studied.[2]

In 2005 it was reported that the chemoselectivity could be completely switched from C=O to C=C bonds in the transfer hydrogenation of activated α,β-unsaturated ketones catalyzed by diamine-ruthenium complex. A wide variety of chiral diamine – Ru(II)-(arene) system was investigated to explore the asymmetric transfer hydrogenation . (i) The structure of the N-sulfonylated chiral diamine ligands, in which several chiral diamines substituted on the benzene ring of DPEN were first reported and (ii) The structure of the metal precursors and high enantioselectivity (upto 89 % ee) at the β carbon atom was obtained.

In 2005, TsDPEN / Ru(II) complexes has proved to be the catalysts of choice as reflected by their applications to date.[29] The best results with TsDPEN / Ru(II) catalysts have been achieved in formic acid / triethylamine,[30] rather than 2-propanol.[31]

In the catalyst, the n^6-arene ring and the diamine ligand are connected through a three-atom-tether.[32] This complex was highly effective at the reduction of acetophenone and other aryl / alkyl ketones.



A new method for the synthesis of tethered amino alcohol - containing catalysts were synthesized.[33]

Objective

To design, synthesize and study transfer hydrogenation using Ru complexes.

Results and Discussion

Rh, Ir, Ru complexes are mostly used for the transfer hydrogenation of ketones using NaOH / KOH as co-catalyst and $HCOONH_4$ and isopropyl alcohol as the two chief reducing agents.

Salen and DMSO complexes of Ru, Rh, Pd have already been used for the hydrogenation of olefins. These complexes are excellent alternatives for the currently used phosphines, ethanol amines, diamines and other ligands, for routine transfer hydrogenation reaction not requiring asymmetric induction as they are readily available non-phosphorus ligands and can be readily synthesized from commercially available precursors with substituents to influence catalytic properties and asymmetric induction. The present work deals with the transfer hydrogenation of acetophenone, benzalacetone, cinnamaldehyde and citral in the presence of $RuCl_2$ $(DAB)_2$, Ru DMSO, Ru DMSO-$P(C_6H_5)_3$ prepared by known procedures and KOH as co-catalyst using i-C_3H_7OH as the transfer hydrogenating agent. These reactions gave excellent yield, and effectively reduced selectively the carbonyl moiety.

Benzoin was reduced to 1,2-diphenylethylene 1,2-diol in excellent yields (91.43%) using $RuCl_2$ $(DMSO)_4$ catalyst in 10 hr with KOH as co-catalyst and isopropanol as the transfer hydrogenating agent.

4-Methoxybenzaldehyde was reduced in only 30 minutes in 92.51% yield using $RuCl_2$ $(DMSO)_4$ as catalyst to 4-methoxybenzyl alcohol.

Cinnamaldehyde was reduced to cinnamyl alcohol in 24 hr in 81.48% yield. Selective reduction was at the carbonyl moiety only. The double bond remain unaffected.

Acetophenone as reduced to phenethyl alcohol in 24 hr and in 84.69% yield using $RuCl_2$ $(DMSO)_3$ $P(C_6H_5)_3$ and the reaction was in room temperature.

4-Phenyl-but-3-en-2-one was effectively reduced to 4-phenyl-but-3-en-2-ol in 88.48% yield in 12 hr at room temperature. There was selective reduction of the C=O group only.

4-Methoxybenzaldehyde was also reduced with $RuCl_2$ $(DMSO)_3$ $P(C_6H_5)_3$ catalyst and KOH as co-catalyst in 91.78% yield at room temperature for 24 hr.

Thus $RuCl_2$ $(DMSO)_3$ $P(C_6H_5)_3$ catalyst reactions were all carried out at room temperature in excellent yield. Thus the catalyst was highly effective, versatile and selective.

Ru $(DAB)_2Cl_2$ catalyzed transfer hydrogenations of acetophenone (79.71%) yield at reflux temperature to yield phenethyl alcohol using KOH as co-catalyst and isopropanol as the hydrogenating solvent.

Reactions were also carried out with Ru $(DAB)_2Cl_2$ with 4-methoxy benzaldehyde to get 4-methoxy benzyl alcohol (86.52% yield), Benzoin to yield (83.61%) of 1, 2-diphenylethylene-1,2-diol at reflux temperature.

Ru (Salen) $P(C_6H_5)_3Cl$ catalyzed the transfer hydrogenation of acetophenone to yield phenethyl alcohol (82.24%) yield in 24 hr, 4-methoxybenzaldehyde to 4-

methoxybenzyl alcohol in (83.47%) yield in 8 hr and benzoin to 2-diphenyl ethylene-1,2-diol in 77.57% yield in 12 hr.

Reactions took a longer time with this catalyst compared to $RuCl_2$ $(DMSO)_4$ catalyst and the yields were comparatively less.

Comparison with Ru(II) catalyst Vs. Ni (II) catalyst

The transfer hydrogenation of ketones and aldehydes were studied using $RuCl_2$ $(DMSO)_4$ and $RuCl_2$ $\{P(C_6H_5)_3\}_3$ catalysts and $NiCl_2$ $\{P(C_6H_5)_3\}_2$ catalyst.

Acetophenone was reduced to α-phenethyl alcohol in 12-18 hr yield (82%) compared to Ni (II) catalyst, which took 30 hr (82%) yield.

Cinnamaldehyde was reduced to cinnamyl alcohol in 24 hr at room temperature (81.48% yield) with Ru (II) catalyst compared with Ni (II) catalyst which took 2 hr at reflux temperature and yield only 51% of cinnamyl alcohol. KOH/NaOH was used as the co-catalyst in both the hydrogenations.

4-Methoxybenzaldehyde was reduced in 30 minutes with Ru (II) catalyst to yield (92.51%) 4-methoxy benzyl alcohol at room temperature compared to Ni (II) catalyst which took 36 hr at reflux temperature to yield (80%) of the product.

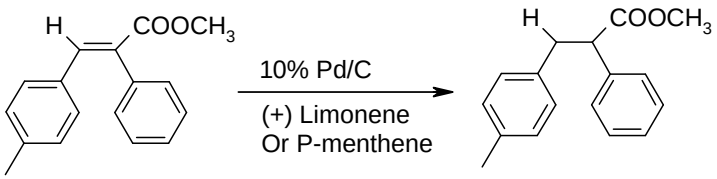
Thus, Ru (II) catalyst was the most efficient and versatile catalyst unlike Ni (II) catalyst which took longer time to reduce ketones and aldehydes. Also reactions proceeded in high yields and lesser time with Ru (II) catalysts, unlike Ni (II) catalysts, which took 12 - 36 hr reaction time and 51 - 82% yield.

Enamino esters are recognized as very useful intermediates for the synthesis of alkaloids.[1] The specific interest of these compounds resides in their poly-functionality, they carry simultaneously a nitrogen atom, a double bond (the reduction of which can

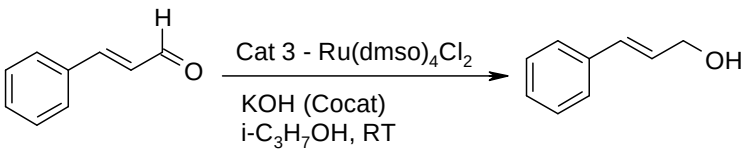
create one or two stereocenters), and an ester moiety which potentially allows extension of the side chain or ring closure.[2] The β-enamino ester moiety is particularly suitable for the synthesis of the nitrogen containing fused bicyclic system present in indolizidine[3] or pyrrolizidine alkaloids, whose chirality is generally located in the α- and β-position of the nitrogen atom. In this context, the reduction of the double bond, which generates the chiral center(s) will be the key step of the sequence in order to obtain the desired stereochemistry of these alkaloids. Several synthetic approaches to natural products have been reported using tri-substituted enamino esters intermediates.[1-4]

Johnstone and Wilby in 1985 attempted to reduce α-acetamido cinnamic acid, which produced only racemic N-acetylphenylalanine.[5] Evidence that optically active donors such as (+)-limonene disproportionate rapidly in the presence of Pd/C was obtained. Reduction of the stilbene in *Scheme-I* gave only a racemic ester in good yield.

Scheme – 1

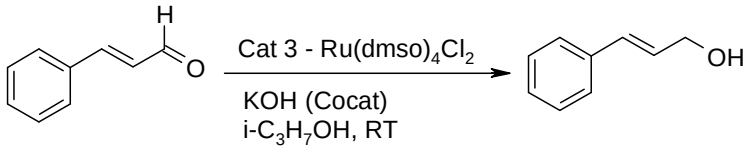


Scheme



Catalyst :1. $Ru(DAB)_2Cl_2$ 2. $Ru(salen)P(C_6H_5)_3Cl$ 3. $Ru(dmso)_4Cl_2$ 4. $Ru(dmso)_3P(C_6H_5)_3Cl_2$

Scheme



Catalyst :1. $Ru(DAB)_2Cl_2$ 2. $Ru(salen)P(C_6H_5)_3Cl$ 3. $Ru(dmso)_4Cl_2$ 4. $Ru(dmso)_3P(C_6H_5)_3Cl_2$

Table-1

Ru DAB (Cat-1), Salen (Cat-2), DMSO (Cat-3) and DMSO-$P(C_6H_5)_3$ (Cat-4) catalyzed transfer hydrogenations[a]

Sr. No.	Carbonyl compound (mmol)	Catalyst (mmol)	Time (hr)	Temp	Yield (%)
1.	$C_6H_5.COCH_3$ (5)	Ru DAB-1 (0.025)	14	reflux	80
2.	$C_6H_5COCH_3$ (3)	Ru Salen.$P(C_6H_5)_3$ –2 (0.04)	10	reflux	82
3.	$C_6H_5.COCH_3$ (2)	Ru (DMSO)-3 (0.1)	8	reflux	85
4.	$C_6H_5COCH_3$ (3)	Ru (DMSO). $P(C_6H_5)_3$-4(0.025)	24	RT	84.7
5.	4-$CH_3O.C_6H_4.CHO$ (5)	Ru DAB-1 (0.025)	10	reflux	86.5
6.	4-$CH_3O.C_6H_4.CHO$ (3)	Ru Salen-2 (0.04)	8	reflux	93
7.	4-$CH_3O.C_6H_4.CHO$ (3)	Ru (DMSO)-3 (0.049)	30 (min)	reflux	92.5
8.	4-$CH_3O.C_6H_4.CHO$ (3)	Ru (DMSO)-3 (0.04)	24	RT	85
9.	4-$CH_3.O.C_6H_4.CHO$ (3)	Ru(DMSO).$P(C_6H_50_3$ –4 (0.025)	24	RT	91.8
10.	$C_6H_5CH=CH.CO.CH_3$ (3)	Ru(DMSO)-3 (0.049)	25 (min)	reflux	96
11.	$C_6H_5.CH=CH.CO.CH_3$ (2)	Ru (DMSO)-3 (0.04)	17	reflux	90
12.	$C_6H_5.CH=CH.CO.CH_3$ (3)	Ru (DMSO).$P(C_6H_5)_3$ -4 (0.025)	12	RT	88.3
13.	$C_6H_5.CH=CH.CHO$ (3)	Ru (DMSO)-3 (0.04)	24	RT	71
14.	Citral (3)	Ru (DMSO)-3 (0.04)	3	RT	86.8

A: Reaction conditions- Acetophenone : 3 mmole, Cat-1 {$RuCl_2$ (DAB} 0.025 mmole, KOH : 0.357 mmole, i-C_3H_7OH : 15 ml, reflux, 14 hr, 80% yield of α-phenethyl alcohol; All reaction products are known compounds and characterized by ^{1}H-NMR and IR.

Preparation of Catalyst

Preparation of Salen Ligand

Salicyclaldehyde (5.1 ml, 41 mmol) in 10 ml methanol was taken in a flask and ethylene diamine (1.5 ml, 2.5 mmol) was added slowly with stirring for 1.5 hr. Yellow crystals of the ligand was obtained by evaporating methanol under reduced pressure. Yield (6.5 g, 58.28 %, m.p. 118°C.

Preparation of $RuCl_2$ $(dmso)_4$

Dichlorotetrakis (dimethyl sulphoxide) ruthenium – II

Ruthenium trichloride trihydrate (1 g) was refluxed in dimethyl sulphoxide (5 ml) for 5 minutes. The volume was reduced to half in vacuo. On addition of acetone (20 ml) gave a yellow precipitate which was separated and filtered, washed with acetone and ether and vacuum dried. Recrystallized from dimethyl sulphoxide by slow evaporation of a hot concentrated solution yielded hexagonal plates (1.33 g, 72% M.P. 193°C decomp)

Preparation of $RuCl_2$ $\{P(C_6H_5)_3\}$ $(dmso)_4$

Dichlorobis (dimethyl sulphoxide) (triphenyl phosphine) ruthenium II

$RuCl_2$ $(dmso)_4$ (0.3 g) was suspended in toluene (40 ml) and triphenyl phosphine (0.325 g) added. The suspension was refluxed for 40 minutes to give orange coloured solution. The toluene was removed, the residue dissolved in minimum of acetone and the buff complex precipitated by addition of ether. The complex was washed and

recrystallized from acetone (20 ml) and ether (20 ml) (0.17 g, 50% yield, M.P. 200°C decomp).

Preparation of DAB Complex of Ru-cis-dichloro-bis (2,7-dimethyl-3,6-diazo-octadiene-3, 5) ruthenium II (2)

Heating of $RuCl_3.3H_2O$ (0.280 g, 1.04 mmol Ru) in tetrahydrofuran (20 ml) with DAB (0.365 g, 2.60 mmol) and slight excess of Zn dust (0.038 g, 0.58 mmol) gave a violet strongly coloured solution after 1 hr of stirring. The solvent was removed and the residue extracted with $CHCl_3$. The product recovered from this solution was dissolved in minimum quantity of acetone and purified by column chromatography on neutral alumina (Me_2CO : Et_2O; 1:1) At -20°C (0.050 g) of dark crystals with a green metallic luster was obtained (0.210 g, 44% yield).

Preparation of $RuCl_2$ $\{P(C_6H_5)_3\}_3$

$RuCl_3$ (0.2 g) in methanol (50 ml) was taken in a flask and 6 fold PPh_3 was added and refluxed under nitrogen for several hours. Reddish brown crystals appeared, which was washed with methanol and ether and dried in vacuo at 60 °C. Yield (75%).

Preparation of Ru (Salen) $\{P(C_6H_5)_3\}Cl$

H_2 salen (1.44 g, 5 mmol) was dissolved in ethanol (100 ml) and excess triethylamine (2 g) was added. The solution was heated to boiling and solid Ru $(PPh_3)_3Cl_2$ (4.79 g, 5 mmol) added. Air was drawn through the hot solution until all the solid had dissolved forming a green solution. The solution was cooled and filtered and evaporated to dryness. The residue was extracted several times with water to remove

$N(C_2H_5)_3$.HCl and with benzene to remove $P(C_6H_5)_3$. Green crystals was formed from the precipitate.

Results and Discussion

Transfer hydrogenation with salen, DAB, Ru complex of acetophenone, anisaldehyde gave 77 - 93 % yield in 8 - 12 hr. Reduction with the DAB Ru (Cat -1) however took longer time. Benzalacetone, cinnamaldehyde, anisaldehyde and citral gave excellent yields with selectivity for the carbonyl group. The reductions of acetophenone, cinnamaldehyde, benzalacetone, anisaldehyde, citral at reflux temperature took 30 minutes – 10 hr compared to 3-23 hr at room temperature.

The Ru $(DMSO)_3$ $P(C_6H_5)_3$ (Cat - 4) complex also gave high yields (84 - 91%) for reduction of acetophenone, benzalacetone and anisaldehyde at room temperature 12 - 24 hr. The results are shown in Table. Ru $(DMSO)_4Cl_2$ complex gave the highest yield for the transfer hydrogenation of acetophenone (85 % yield in 8 hr) and anisaldehyde (92.5 % yield in 25 minutes) at 110-120 °C. Benzalacetone (96 % yield in 25 minutes) also gave the highest yields in the shortest reaction times with this catalyst.

Thus catalyst 3, that is Ru $(DMSO)_4Cl_2$ transfer hydrogenation atom as it gave excellent yields at a very short reaction time than other Ru catalysts.

Acetophenone, anisaldehyde, benzalacetone, citral and citronellal were reduced with Ru DAB, Ru (DMSO), Ru Salen $P(C_6H_5)_3$ and Ru DMSO $P(C_6H_5)_3$ catalysts. There was selective reduction at the carbonyl moiety. The double bond of the olefin was not reduced in benzalacetone, citral, citronellal.

Acetophenone was reduced to α-phenethyl alcohol in 80% yield with Ru DAB catalyst at reflux temperature in 14 hr. When Ru Salen $P(C_6H_5)$ was used as the catalyst acetophenone was reduced in 82% yield and at 10 hr reflux temperature. Excellent results were obtained with catalyst Ru (DMSO). $P(C_6H_5)_3$ and Ru (DMSO) catalyst. The yield obtained was 85%.

4-Methoxy benzaldehyde were also reduced at the carbonyl moiety with the above catalysts. Ru (DMSO) catalyst giving excellent results 92.5% yield in 30 minutes.

Citral and citronellal were selectively reduced with catalyst Ru (DMSO) at room temperature to yield geraniol and citronellal in 86.8% yield. The reactions with Ru (DMSO) catalyst were at room temperature concluding that Ru $(DMSO)_4Cl_2$ and Ru $(DMSO)_3P(C_6H_5)_3Cl_2$ were excellent ruthenium catalysts for the selective transfer hydrogenations.In all these reactions, isopropanol was the chief hydrogenating agent and KOH used as the co-catalyst.

Synthetic Applications

Asymmetric transfer hydrogenations of α acetamido cinnamic acid esters were catalyzed by rhodium complexes like [Rh (COD) BF_4, [Rh (S-momophos) (COD)]BF_4, BINAPO ligands, BINAP,DIOP,CHIRAPHOS,Aminophosphinite complexes in isopropanol or methanol as the solvent to get N-acetylphenylalanine with high enantioselectivities (86-98%) ee was obtained.[13-23]

We decidie to carry out the asymmetric transfer hydrogenation of β enamidoesters with various ruthenium and rhodium complexes to get the double bond reduction or formation of β lactams on intramolecular cyclization as both these

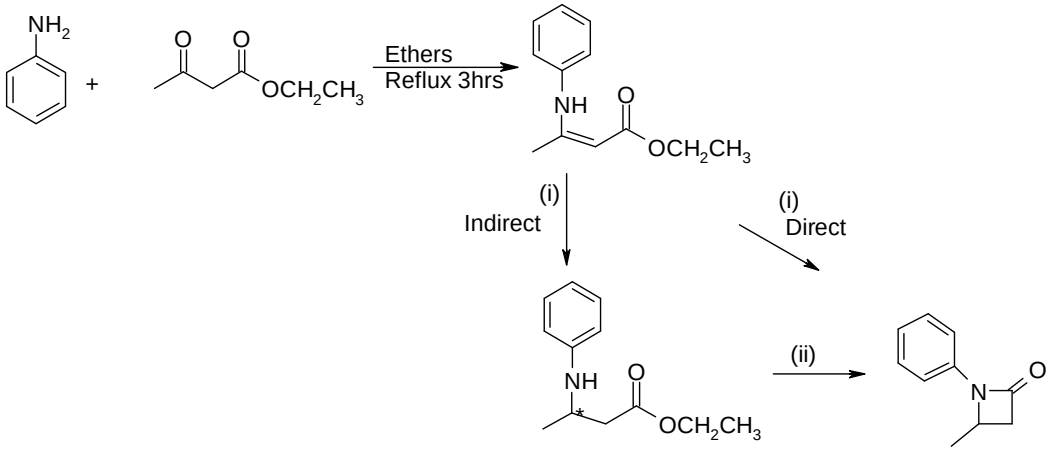
molecules are chiral and are important in pharmaceuticals and exhibit medicinal properties in antibiotics.

Our aim was to do transfer hydrogenation of β-enamido esters which will lead to the formation of β-acetamido esters and intramolecular cyclization or intra molecular condensation, which will result in the formation of β-lactams. The process can be asymmetric because we start with a prochiral enamide. These enamine esters can be easily synthesized from β-keto esters and amines. Both these molecules are important constituents of antibiotics and have medicinal properties.

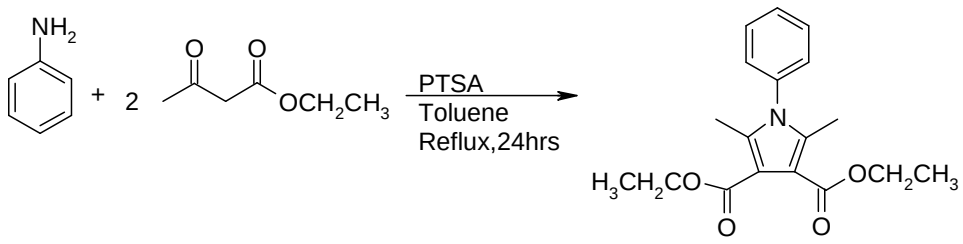
β-Keto esters are ambidient electrophiles for condensation with amines, but the greater reactivity of ketone than ester co-groups leads to the preferential formation of enamine esters in most cases.

Oxidation of β-amine cinnamates to pyrroles were observed when two equivalent of β-keto esters were used under modified conditions

Scheme



β-Ketoester β-Lactam



Attempts were made to transfer hydrogenated β-acetamido esters using 10% Pd/C, $PdCl_2$ $[P(C_6H_5)_3]_2$, $RuCl_2$ $[P(C_6H_5)_3]_3$ and Rh(COD) as catalysts using $HCOONH_4$ and isopropanol as the chief transfer hydrogenating agents. The reactions were refluxed for 3-24 hr. However, there was no product seen after purification on column chromatography.

Reactions were also attempted using the above catalysts using methanol and pressure hydrogen balloon. However, there was no product seen.

The double bond could not be reduced nor could we get the β-lactam formation.

In pursuing the study of transfer hydrogenation of β-acetamidoesters, we are designing new catalysts and reaction conditions.

Conclusion

Further attempts are in progress for the transfer hydrogenation of β-acetamido esters using ruthenium and rhodium catalysts.

Ru $(DMSO)_3$ $P(C_6H_5)_3$ (Cat - 4) complex and Ru $(DMSO)_4Cl_2$ complex gave the highest yield for the transfer hydrogenation of acetophenone, benzal acetone and anisaldehyde and were carried out at room temperature. Ru $(DMSO)_4Cl_2$ complex gave the highest yield (85 - 96 % yield). The transfer hydrogenation of acetophenone, benzalacetone and anisaldehyde. Thus effectively and selectively reducing the carbonyl moiety.

Thus sulphoxides, salen and DAB are excellent ligands for Ru catalyzed transfer hydrogenation. Asymmetric induction in transfer hydrogenations with chiral ligands and catalysts would be extremely facile with opportunity for easy variations in functional group substitutions in the ligands to affect both reactivity and selectivity.

Experimental

1. $RuCl_2$ $(DMSO)_4$ catalyzed transfer hydrogenation of acetophenone using isopropyl alcohol

Acetophenone (0.240 g, 2 mmol), Ru $(DMSO)_4Cl_2$ (cat-3, 0.048 g, 0.1 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst, were taken in a flask containing 15 ml I-C_3H_7OH and refluxed for 8 hr under argon. Evaporated solvent on a rotavap, diluted with water, extracted (ethylacetate – 3 x 25 ml), followed by concentration and purification by column chromatography over silica gel (100 - 200 mesh) gave 0.208 g (85% yield) of α-phenethyl alcohol.

B.P. : 83-84°C/9mm of Hg

IR (cm^{-1}): 3320, 2980, 2940, 2900, 2800, 2460, 1960, 1895, 1615, 1505, 1460, 1380, 1225, 1070, 1020, 910, 750.

^{1}H-NMR (δ, $CDCl_3$, 80 MHz): 7.23 (m, 5H, Ar), 4.83-4.5 (q, 8Hz, 1H, CH.CH_3), 4.0 (s, 1H, OH), 1.3-1.2 (d, 8Hz, 3H, CH.CH_3).

2. $RuCl_2$ $(DMSO)_4$ catalyzed transfer hydrogenation of 4-phenylbut-3-en-3-2-one using isopropanol

4-Phenylbut-3-en-2-one (0.291 g, 2 mmol), Ru $(DMSO)_4Cl_2$ (Cat - 3, 0.048 g, 0.1 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst, were taken in a flask containing 15 ml i-C_3H_7OH and refluxed for 25 minutes under argon. Evaporated the solvent on rotavap, diluted with water, extracted (ethyl acetate – 3 x 25 ml), followed by concentration and purification by column chromatography over silica gel (100 - 200 mesh) gave 0.478 g (96 % yield) of 4-phenyl-but-3-en-2-ol.

3. $RuCl_2$ $(DMSO)_4$ catalyzed transfer hydrogenation of citral using isopropyl alcohol

Citral (0.304 g, 2 mmol), Ru $(DMSO)_4Cl_2$ (cat - 3, 0.048 g, 0.1 mmol), KOH (0.020 g, 0.357 mmol) as co-catalysts, were taken in a flask containing 15 ml i-C_3H_7OH and stirred at room temperature for 3 hr under argon. Evaporated solvent on rotavap, diluted with water, extracted (ethyl acetate – 3 x 25 ml), followed by concentration and purification by column chromatography over silica gel (100 - 200 mesh) gave 0.267 g (86.8% yield) of geraniol.

IR (cm^{-1}): 3300, 2800, 1430, 1370, 1050, 1000

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 5.45-5.32 (t, 6Hz, 1H, C=C<u>H</u>.CH_2), 5.15-5.05 (t, 6Hz, 2H, C=<u>CH</u>.CH_2), 4.16-4.13 (d, 6Hz, 2H, <u>CH_2</u>OH), 1.60 (s, 6H, CH=C(C<u>H_3</u>)$_2$), 1.50-1.05 (m, 4H, CH.<u>CH_2</u>.<u>CH_2</u>.C=), 0.90-0.87 (s, 6Hz, 3H, C.C<u>H_3</u>).

4. $RuCl_2$ $(DMSO)_4$ catalyzed transfer hydrogenation of citronellal using isopropyl alcohol

Citronellal (0.304 g, 2 mmol), Ru $(DMSO)_4Cl_2$ (Cat - 3, 0.048 g, 0.1 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst, were taken in a flask containing 15 ml i-C_3H_7OH and stirred at room temperature for 4 hr under argon. Evaporated solvent on a rotavap, diluted with water, extracted (ethyl acetate – 3 x 25 ml), followed by concentration and purification by column chromatography over silica gel (100 - 200 mesh) gave (86% yield), 0.268 g of citronellal.

IR (cm^{-1}): 3200, 2800, 1650, 1390, 1320, 1000, 450

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 5.15-5.05 (m, 1H, C=C<u>H</u>.CH_2), 3.72-3.60 (m, 2H, <u>CH_2</u>OH), 2 (m, 2H, <u>CH_2</u>), 1.68 (s, 3H, <u>CH_3</u>), 1.58 (s, 3H, CH_3), 1.40-1.1 (m, 4H, C.C<u>H_2</u>.<u>CH_2</u>.C), 0.9-0.8 (m, 4H, =C.<u>CH_3</u> and C<u>H</u>.$(CH_3)_2$).

5. $RuCl_2$ $(DMSO)_4$ catalyzed transfer hydrogenation of Benzoin using isopropanol

Benzoin (2-hydroxy-2-phenyl acetophenone) (0.636 g, 3 mmol), Ru $(DMSO)_4Cl_2$ (Cat-3, 0.048 g, 0.1 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst were taken in a

flask containing (15 mL) i-C_3H_7OH and stirred at room temperature for 10 hr under argon. Evaporated solvent on rotavap, diluted with water, extracted ethyl acetate (3 x 25 ml), followed by concentration and purification by column chromatography over silica gel (100 - 200 mesh) gave 0.587 g (91.43 % yield) of 1, 2-diphenyl ethylene-1,2-diol.

6. $RuCl_2$ $(DMSO)_4$ catalyzed transfer hydrogenation of Benzil using isopropanol

Benzil (0.630 g, 3 mmol), Ru $(DMSO)_4Cl_2$ (Cat - 3, 0.048 g, 0.1 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst were taken in a flask containing 15 mL i-C_3H_7OH and reflux at 110°C for 6 hr under argon. Evaporated solvent on rotavap, diluted with water, extracted (ethyl acetate – 3 x 25 ml), followed by concentration and purification by column chromatography over silica gel (100 - 200 mesh) gave 0.586 g (91.27%) yield of 1, 2 - diphenylethylene-1,2-diol.

7. $RuCl_2$ $(DMSO)_4$ catalyzed transfer hydrogenation of anisaldehyde using isopropanol

Anisaldehyde (0.408 g, 3 mmol), Ru $(DMSO)_4Cl_2$ (Cat - 3, 0.048 g, 0.1 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst were taken in a flask containing 15 mL i-C_3H_7OH and stirred at room temperature for 30 minutes under argon. Evaporated solvent on rotavap, diluted with water, extracted (ethyl acetate – 3 x 25 ml), followed by concentration and purification by column chromatography over silica gel (100 - 200 mesh) gave 0.383 g (92.51% yield) of *p*-methoxy-benzyl alcohol.

8. $RuCl_2$ $(DMSO)_4$ catalyzed transfer hydrogenation of cinnamaldehyde using isopropanol

Cinnamaldehyde (0.396 g, 3 mmol), Ru $(DMSO)_4Cl_2$ (Cat - 3, 0.048 g, 0.1 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst were taken in a flask containing 15 mL i-C_3H_7OH and stirred at room temperature for 24 hr under argon. Evaporated solvent on rotavap, diluted with water, extracted (ethyl acetate – 3 x 25 ml), followed by concentration and purification by column chromatography over silica gel (100-200 mesh) gave 0.286 g of cinnamaldehyde (81.48 % yield).

9. $RuCl_2$ $(DMSO)_4$ catalyzed transfer hydrogenation of cyclohexanone using isopropanol

Cyclohexanone (0.294 g, 3 mmol), Ru $(DMSO)_4Cl_2$ (Cat - 3, 0.048 g, 0.1 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst were taken in a flask containing 15 mL i-C_3H_7OH and refluxed for 24 hr at 110°C under argon. Evaporated solvent on rotavap, diluted with water, extracted (ethyl acetate – 3 x 25 ml), followed by concentration and purification by column chromatography over silica gel (100 - 200 mesh) gave 0.289 g of cyclohexanol in 95.69% yield.

10. $RuCl_2$ $(DMSO)_4$ catalyzed transfer hydrogenation of cyclohexanone using isopropanol

Acetophenone (0.360 g, 3 mmol), $RuCl_2$ $(DMSO)_3P(C_6H_5)_3$ (Cat - 4, 0.325 g,

0.025 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst were taken in a flask containing 15 mL i-C_3H_7OH and stirred at room temperature for 24 hr under argon. Evaporated solvent on rotavap, diluted with water, extracted (ethyl acetate – 3x25 ml), followed by concentration and purification by column chromatography over silica gel (100 - 200 mesh) gave 0.310 g of α-phenethyl alcohol in 84.69% yield.

11. $RuCl_2$ $(DMSO)_3$ $P(C_6H_5)_3$ catalyzed transfer hydrogenation of 4-phenylbut-3-en-2-one using isopropanol

4-Phenylbut-3-en-2-one (0.438 g, 3 mmol), $RuCl_2$ $(DMSO)_3$ $P(C_6H_5)_3$ (Cat-4, 0.325 g, 0.025 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst were taken in a flask containing 15 mL i-C_3H_7OH and stirred at room temperature for 12 hr under argon. Evaporated solvent on rotavap, diluted with water, extracted (ethylacetate – 3x25 mL), followed by concentration and purification over silica gel gave 0.392 g of 4-phenyl-but-3-en-2-ol in (88.48% yield).

12. $RuCl_2$ $(DMSO)_3$ $P(C_6H_5)_3$ catalyzed transfer hydrogenation of anilaldehyde using isopropanol

Anisaldehyde (0.408 g, 3 mmol), $RuCl_2$ $(DMSO)_3$ $P(C_6H_5)_3$ (Cat-4, 0.325 g, 0.025 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst were taken in a flask containing 15 mL i-C_3H_7OH and stirred at room temperature for 24 hr under argon. Evaporated solvent on rotavap, diluted with water, extracted (ethyl acetate – 3x25 mL), followed by

concentration and purification over silica gel gave (0.380 g) of 4-methoxybenzyl alcohol in (91.78% yield).

13. Ru $(DAB)_2Cl_2$ catalyzed transfer hydrogenation of acetophenone using isopropanol

Acetophenone (0.620 g, 5 mmol), Ru $(DAB)_2Cl_2$ (Cat-1, 0.325 g, 0.025 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst were taken in a flask containing 15 mL i-C_3H_7OH and refluxed at 110°C

14. Ru $(DAB)_2Cl_2$ catalyzed transfer hydrogenation of anilaldehyde using isopropanol

Anisaldehyde (0.680 g, 5 mmol), Ru $(DAB)_2Cl_2$ (Cat-1, 0.325 g, 0.025 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst were taken in a flask containing 15 mL i-C_3H_7OH and refluxed at 110°C for 10 hr under argon. Evaporated solvent on rotavap, diluted with water, extracted (ethylacetate – 3 x 25 mL), followed by concentration and purification over silica gel (100-200 mesh) gave 0.597 g of 4-methoxy-benzyl alcohol in (86.52% yield).

15. Ru $(DAB)_2Cl_2$ catalyzed transfer hydrogenation of benzoin using isopropanol

Benzoin (1.060 g, 5 mmol), Ru $(DAB)_2Cl_2$ (Cat-1, 0.325 g, 0.015 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst were taken in a flask containing 15 mL of i-

C_3H_7OH and refluxed at 110°C for 14 hr under argon. Evaporated solvent on rotavap, diluted with water, extracted (ethylacetate – 3 x 25 mL), followed by concentration and purification over silica gel gave 0.893 g of 1,2-diphenylethylene-1,2-diol in (83.61% yield).

16. Ru (Salen) $P(C_6H_5)_3Cl$ catalyzed transfer hydrogenation of acetophenone using isopropanol

Acetophenone (0.360 g, 3 mmol), Ru (Salen) $P(C_6H_5)_3Cl$ (Cat-2, 0.024 g, 0.04 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst were taken in a flask contaiing 15 mL of i-C_3H_7OH and refluxed at 24 hr under argon. Evaporated solvent on rotavap, diluted with water, extracted (ethylacetate – 3 x 25 mL), followed by concentration and purification over silica gel (100 - 200 mesh) gave 0.301 g of phenethyl alcohol in (82.24 % yield).

17. Ru (Salen) $P(C_6H_5)_3Cl$ catalyzed transfer hydrogenation of 4-methoxy benzaldehyde

4-Methoxybenzaldehyde (0.408 g, 3 mol), Ru (Salen) $P(C_6H_5)_3Cl$ (Cat - 2, 0.024 g, 0.04 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst were taken in a flask ontaining 15 mL of i-C_3H_7OH and refluxed at 110°C for 8 hr under argon. Evaporated solvent on rotavap, diluted with water, extracted (ethylacetate – 3 x 25 ml), followed by concentration and purification over silica gel gave 0.387 g of 4-methoxybenzyl alcohol in (93.47% yield).

18. Ru (Salen) $P(C_6H_5)_3Cl$ catalyzed transfer hydrogenation of Benzoin

Benzoin (0.636 g, 3 mmol), Ru (Salen) $P(C_6H_5)_3Cl$ (Cat - 2, 0.024 g, 0.04 mmol), KOH (0.020 g, 0.357 mmol) as co-catalyst were taken in a flask containing 15 mL i-C_3H_7OH and refluxed at 110°C for 12 hr under argon. Evaporated solvent on rotavap, diluted with water, extracted (ethylacetate – 3 x 25 mL), followed by concentration and purification over silica gel gave 0.498 g of 2-diphenylethylene-1,2-diol in (77.57% yield).

Preparation of catalyst $RuCl_2$ $[P(C_6H_5)_3]_3$

$RuCl_3.3H_2O$ (1.0 g, 3.8 mmol) was dissolved in methanol (250 ml) and the solution was refluxed under nitrogen for 5 minutes. The mixture was then cooled and $P(C_6H_5)_3$ was added (6.0 g, 22.9 mmol) in ratio of 6:1. The reaction mixture was refluxed for 3 hr under nitrogen. The complex precipitate formed from the hot solution was in the form of dark black crystals. The mixture was cooled and filtered under nitrogen, washed with ether and dried in vacuo. 2.7 g (75%) yield of the catalyst. M.P. 132-134 °C.

Preparation of β-acetamido ester

To a solution of ethyl acetoacetate (0.186 g, 2 mmol) in ether (15 mL) cooled to –5°C was added dropwise aniline (0.260 g, 2 mmol) under stirring for 3.5 hr and the reaction was monitored on TLC. The reaction mixture was then evaporated on rotavap and washed with ethyl acetate and water (3 x 15 mL). The combined organic extracts was then dried in sodium sulphate and the solvent evaporated and column

chromatographed with (100 - 200 mesh) silica gel and purified to get β-acetamide ester in 80% yield.

Preparation of 1-phenyl-3,4-diethyl carboxylate pyrrole

In a round bottom flask aniline (0.093 g, 1 mmol) and ethyl acetoacetate (0.260 g, 2 mmol) were refluxed in toluene 15 mL azeotropically. *p*-toluene sulphonic acid (0.028 g) was added catalytically and the reaction was refluxed to 110 °C for 24 hr. The reaction was monitored on TLC. Toluene was evaporated on rotavap and the reaction mixture was extracted with (3 x 15 mL) ethyl acetate and washed with brine. The combined organic extracts were dried in anhydrous sodium sulphate and solvent evaporated and chromatographed to get the product in 65% yield.

Transfer hydrogenation of β-acetamido ester using 10% Pd/C and $HCOONH_4$

A solution of β-acetamido ester (0.206 g, 1 mmol), 10% Pd/C (0.1 mmol, 10 mole %), $HCOONH_4$ (0.318 g, 5 mmol) was refluxed in isopropanol for 24 hr. The reaction mixture was monitored by TLC. However, the reaction did not go to completion as the substrate was still visible on TLC even after 24 hr of refluxing in C_3H_7OH.

Transfer hydrogenation of β-acetamido ester using $PdCl_2$ $P[(C_6H_5)_3]_2$ and $HCOONH_4$

A solution of β-acetamido ester (0.206 g, 1 mmol), $PdCl_2$ $P(C_6H_5)_3$ (0.1 mmol, 10 mol %), $HCOONH_4$ (0.318 g, 5 mmol) was refluxed in CH_3OH (15 mL) for 24 hr. The reaction mixture was monitored by TLC. However, there was no change in the reaction after 24 hr of reflux.

Transfer hydrogenation of β-acetamido ester using $RuCl_2$ $[P(C_6H_5)_3]_3$ and $HCOONH_4$

A solution of β-acetamido ester (0.206 g, 1 mmol), $RuCl_2$ $\{P(C_6H_5)_3\}_3$ (0.025 g), $HCOONH_4$ (0.318 g, 5 mmol) was refluxed in CH_3OH (15 mL) for 24 hr under pressure hydrogen balloon attached to the flask. The reaction was monitored on TLC. However, there was no change in the starting material even after 24 hr of reflux.

Transfer hydrogenation of β-acetamido ester using Rh(COD) and $HCOONH_4$

A solution of β-acetamido ester (0.206 g, 1 mmol) Rh(COD) catalyst (0.1 mmol 10 ml %), $HCOONH_4$ (0.318 g, 5 mmol) was refluxed in CH_3OH (15 mL) for 24 hr under pressure hydrogen. The reaction was monitored on TLC. However, there was no change in the substrate on TLC.

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Chapter - 3

Introduction

Catalytic transfer hydrogenation has gained tremendous importance in the laboratory for the reduction of various functional groups. $HCOONH_4$ and isopropyl alcohol are two of the most common reducing agents. The dramatic accelerating effect of NaOH / KOH as co-catalyst for the transfer hydrogenation of ketones using Ru catalyst was demonstrated by Backvall *et al*.[2] Rh, Ir and Ru complexes are mostly used for such reductions.[3]

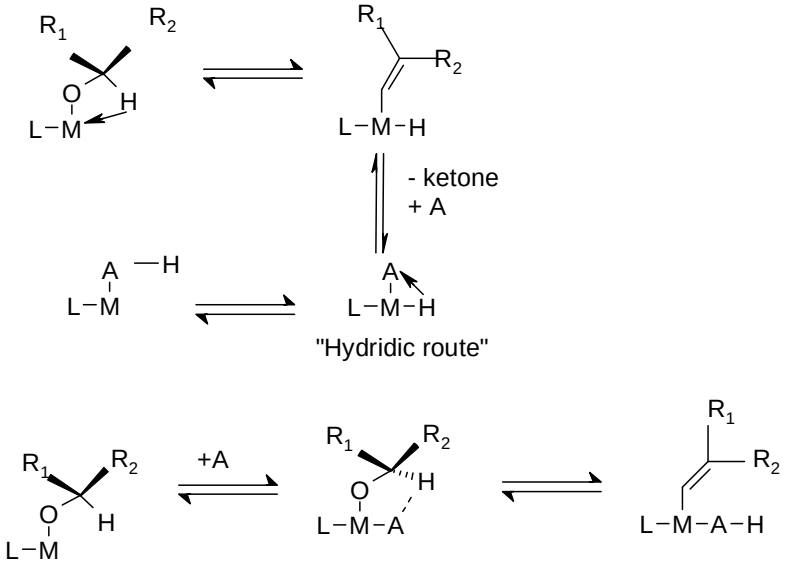
$NiCl_2\{P(C_6H_5)_3\}_2$ has been used to catalyze the hydrogenation of olefins.[6] Raney-Ni has been used as a catalyst for the transfer hydrogenation of ketones using isopropyl alcohol $NiCl_2\{P(C_6H_5)_3\}_2$ catalyze the transfer hydrogenation of aldehydes and ketones using isopropyl alcohol with NaOH/KOH as co-catalyst.[8] No reaction occurs in the absence of co-catalyst. The transfer hydrogenation reductions using $HCOONH_4$ as reducing agent was catalyzed by $Ni\{P(OC_6H_5)_3\}_4$, the first example of a non-halide metal complex catalyst.[9] The use of Ni salts and catalysts for transfer hydrogenation in alkaline medium has been described.[10]

Ni(0) complexes are known to form NiH species in the presence of acid and are used for the isomerisation of olefins.[11] Such species can also be generated by the oxidative addition of Ni(0) to isopropyl alcohol, $HCOONH_4$ and used for transfer hydrogenation reactions. $Ni\{P(OC_6H_5)_3\}_4$ is an air stable and readily available catalyst and forms NiH species in the presence of acids. We have earlier demonstrated the use of this catalyst for oxidative addition reactions to aryl iodides.[12] There is no report to date

on the use of a homogenous catalyst in the zero oxidation state for transfer hydrogenation reactions, which should facilitate such reaction and the oxidative addition of these metal complexes to the reducing agent would be an excellent method for generating the NiH species.

Asymmetric transfer hydrogenations have been carried out using chiral ligands.[4] From a mechanistic point of view, two general reaction paths can be envisaged for hydrogen transfer.

Zassinovich *et al.* in 1975 devised a stepwise process called “hydridic route”, and a concerted process called “direct hydrogen transfer” as shown in *Figure-1*.



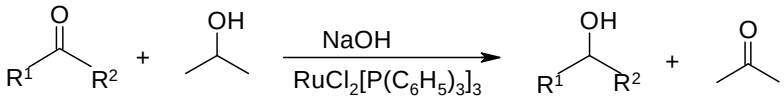
L = Chiral or achiral ligand

A = Substrate having a pro-chiral center

Thus the basic ways by which enantioselective hydrogen transfer can be achieve are enantioface selection by means of a chiral catalyst on achiral (prochiral) substrates or enantiomer selection of a chiral racemic compound.

Backvall *et al*. in 1991 showed that in the presence of the co-catalyst NaOH (2.4 Mol %), $RuCl_2$ $(P(C_6H_5)_3)_3$ (0.1 mol %) catalyzed efficiently. The transfer hydrogenation of both aliphatic and aromatic ketones by propan-2-ol with rates of 900 turnovers per hour at 82 °C, no hydrogenation occurs in the absence of NaOH.

Scheme – 1



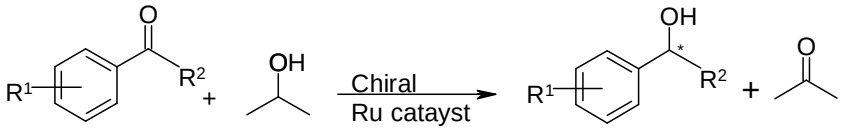
The role of the base is to generate a more nucleophilic alkoxide ion, which would rapidly attack the Ru complex responsible for dehydrogenation. With propan-2-ol, there is no decarbonylation, therefore, catalyst lifetime is long.

Imines also were readily transfer hydrogenated by propan-2-ol in the presence of $RuCl_2$ $(PPh_3)_3$ and base.

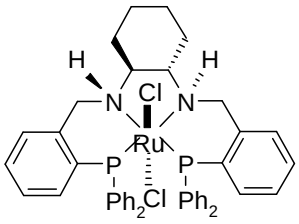
Asymmetric transfer hydrogenation of a range of aromatic ketones in 2-propanol using iridium (I) complexes prepared from $[IrCl(cod)]_2$ and a variety of chiral diamine ligands derived from α-amino acids.

Noyori et al. in 1997 showed the asymmetric reduction of C=O and C=N bonds forming chiral alcohols and amines using 2-propanol. High enantio selectivity was obtained when an appropriate arene and chiral amino alcohol were combined and KOH as co-catalyst.

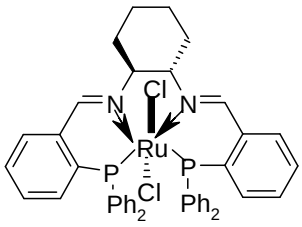
Scheme - 3



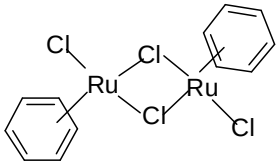
Catalysts: tetra dentate diphosphine / diamine ligand and $[RuCl_2 (n^6\text{-benzene})]_2$



(S,S) -1



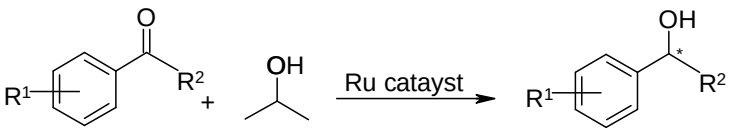
(S,S) -2



[3]

In 1996 a ruthenium (II) complex, (1S,2S)-2-methylamino-1,2-diphenyl ethanol and KOH serves as an efficient catalyst for asymmetric transfer hydrogenation of acetophenone derivatives in propan-2-ol to give (S) enriched alcohols in up to 92 % ee.

Scheme – 4



a R^1 = H, R^2 = Me

b R^1 = H, R^2 = Et

c R^1 = H, R^2 = $CHMe_2$

d R^1 = H, R^2 = Cme_3

e R^1 = O-Me, R^2 = Me

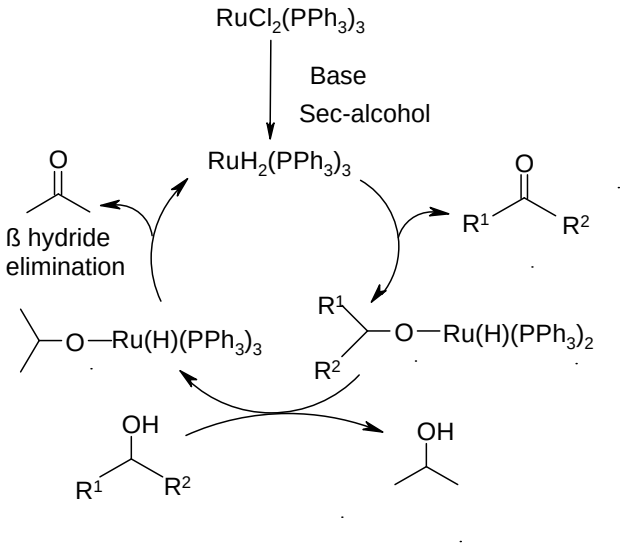
f R^1 = O-Cl, R^2 = Me

g R^1 = p-OMe, R^2 = Me

Noyori *et al*. in 1995 showed the asymmetric transfer hydrogenation of aromatic ketones catalyzed by Chiral Ruthenium (II) complexes. Acetophenone and propiophenone were reduced to >97% optical yield. A *p*-methoxy group in aceto phenone decreases the enantioselectivity, whereas *m*-chloroacetophenone achieved the best result 98 % ee.

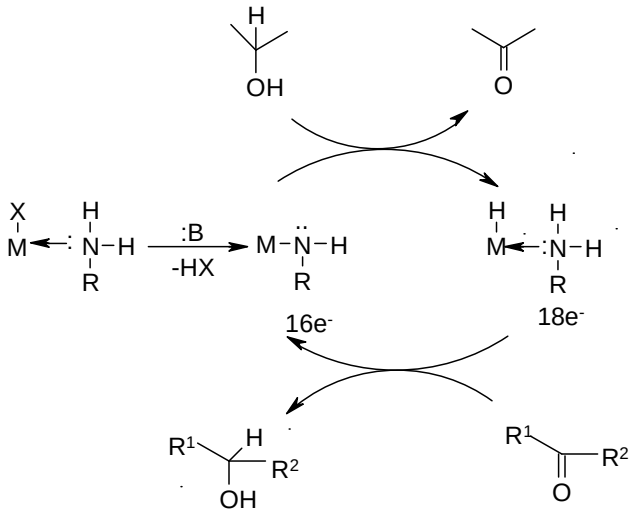
Backvall *et al*. in 1999 gave evidence for a ruthenium dihydride species as the active catalyst in the $RuCl_2$ {PPh_3}-catalyzed hydrogen transfer reaction in the presence of a base *via* two consecutive alkoxide displacement and β-elimination sequences.

Mechanism of $RuCl_2$ $(PPh)_3$-catalyzed hydrogen transfer



The monohydride species did not react with acetone whereas the dihydride reduced acetone to isopropanol where there is a large excess of alcohol, it is likely that proton transfer from isopropanol to the alkoxy group in 6 takes place. This leads to an exchange of alkoxy groups on ruthenium to give 7.

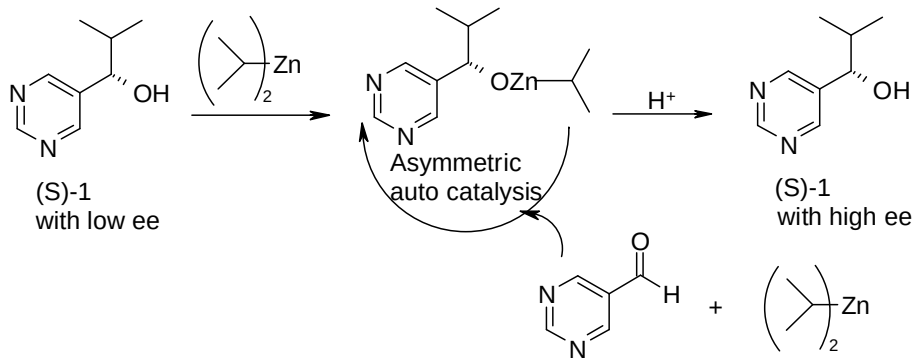
Noyori *et al*. in 2001 gave further evidence that a substrate / metal complexation is not always necessary for hydrogenative saturation of unsaturated compounds. The metal ligand bifunctional mechanism allows for direct reduction of carbonyl compounds with an 18-electron transition metal hydride without C=O / metal interaction Asymmetric transfer hydrogenation of aromatic carbonyl compounds using a 2-propanol / alkaline base system in the n^6-arene ligand gives the corresponding S chiral alcohols of high enantiomeric purity. The reaction proceeds *via* a saturated 18-electron complex. The hydridic RuH and protic NH are simultaneously delivered to a C=O linkage *via* a six-membered pericyclic mechanism giving an S alcohol and 16-electron Ru amide complex which dehydrogenates 2-propanol to regenerate the Ru hydride species. A formic acid / triethylamine mixture serves as a better reducing agent.



Soai *et al.* in 1995 proposed a reaction scheme of auto-catalysis and inhibition in a system of replicating chiral molecules in an initially racemic mixture to yield almost exclusively one enantiomer.

When a 5-pyrimidyl alkanol with a small (2%) enantiomeric excess is treated with diisopropyl zinc and pyrimidine-5-carboxaldehyde, it undergoes an auto-catalytic reaction to generate more of the alkanol. As the reaction involves a chiral catalyst generated from the initial alkanol and because the catalytic step is enantioselective, the enantiomeric excess of the product is enhanced.

Scheme- 6



In 1997 an alternative conceptually opposite strategy to asymmetric catalysis in which a chiral activator selectively activated one enantiomer of a racemic chiral catalyst titanium IV complex for which a chiral additive acts as the chiral activator.

Objective

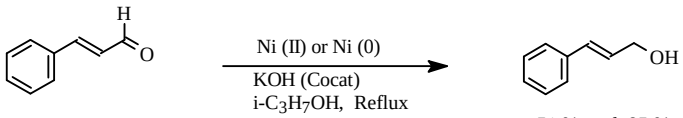
Our aim was to reduce α,β-unsaturated ketones and aldehydes in the presence of NaOH or KOH as co-catalyst and $NiCl_2\{P(OC_6H_5)_3\}$ which are $Ni\{P(OC_6H_5)_3]_4$ and Ni (II) catalysts and compare their catalytic activity. We report the first use of racemic and chiral ligands like phenyl glycine and phenyl glycinol with $Ni\{P(OC_6H_5)_3\}_4$ as catalyst for the transfer hydrogenation of acetophenone.

Results and Discussions

The transfer hydrogenation of ketones and aldehydes using isopropyl alcohol was catalyzed by $NiCl_2$ $\{P(C_6H_5)_3\}_2$ and Ni $\{P(OC_6H_5)_3\}_4$ with NaOH/KOH as co-catalyst. $HCOONH_4$ was also an efficient reducing agent in the presence of Ni (0) catalyst. Ni $\{P(OC_6H_5)_3\}_4$ is the first example of a non-halide transition metal complex used for transfer hydrogenation. This is also the first example of a non-halide transition metal complex used for transfer hydrogenation. This is also the first example of a preliminary oxidative addition mechanism for transfer hydrogenation reactions. The selective reduction of the carbonyl moiety in α, β-unsaturated carbonyl compounds could be carried out using these Ni catalysts. Reductions using isopropyl alcohol could be carried out at room temperature with ethanol amine as ligand. Transfer hydrogenation of acetophenone using racemic ligands were first reported to give asymmetric induction of 4.7 and 2.68 % ee. Aromatic aliphatic ketones, keto esters, aldehydes were easily reduced to the alcohols. α,β-unsaturated aldehydes were reduced selectively to unsaturated alcohols.

The reduction of ketones and aldehydes was studied with $NiCl_2$ $\{P(C_6H_5)_3\}_2$ as catalyst and was possible only in the presence of NaOH/KOH as co-catalyst. Aromatic aliphatic ketones, keto esters, aldehydes were easily reduced to the alcohols. α,β-unsaturated aldehydes were reduced selectively to unsaturated alcohols. Aldehydes were reduced faster than ketones and the reactions were dependent on the concentration of NaOH. The results are shown in Table-1.

Scheme



51 % and 95 %

Ni (II) : $NiCl_2\{P(C_6H_5)_3\}_2$; Ni (0) : $Ni\{P(OC_6H_5)_3\}_4$

Table-1 : $NiCl_2\{P(C_6H_5)_3\}_2$ – Ni (II) - catalyzed transfer hydrogenation of aldehydes and ketones using $i\text{-}C_3H_7OH$

S. No.	Substrate	Time, h	Product	Yield, (%)
1.	$C_6H_5.CO.CH_3$	30	$\tilde{\alpha}\text{-}C_6H_5.CHOH.CH_3$	82
2.	$4\text{-}CH_3.C_6H_4.CO.CH_3$	36	$\tilde{\alpha}\text{-}4\text{-}CH_3).C_6H_5.CHOH.CH_3$	80
3.	$4\text{-}Cl.C_6H_4.CO.CH_3$	24	$\tilde{\alpha}\text{-}4\text{-}Cl).C_6H_5.CHOH.CH_3$	77
4.	$\alpha\text{-}C_{10}H_{10}O$	36	$\alpha\text{-}C_{10}H_{11}OH$	65
5.	$C_6H_5.CO.COOCH_3$	36	$C_6H_5.CHOH.COOCH_3$	65
6.	$C_6H_{10}O$	24	$C_6H_{11}OH$	56
7.	$4\text{-}t\text{-}C_{10}H_{18}O$	20	$4\text{-}t\text{-}C_{10}H_{19}OH$	56
8.	$C_{13}H_{26}O$	24	$C_{13}H_{27}OH$	72
9.	$4\text{-}CH_3O.C_6H_4.CHO$	12	$4\text{-}CH_3O.C_6H_4.CH_2OH$	76
10.	$C_6H_5.CH{=}CH.CHO$	30	$C_6H_5.CH{=}CH.CH_2OH$	51
11.	$C_9H_{17}CHO$ (Citronellal)	24	$C_9H_{17}CH_2OH$ (Citronellol)	57

The double bond in ethyl cinnamate was not reduced by this catalyst. 2-Methyl cyclohexanone formed trans 2-methyl cyclohexanol as the product. An imine, (4-methoxy benzylidene aniline) and a nitro compound (4-nitro toluene) could also be reduced but nitrile was unreactive. The results of this reduction are presented in Table2

Table-2: $Ni\{P(OC_6H_5)_3\}_4$-Ni (0) - Catalyzed transfer hydrogenation using $HCOONH_4$

S. No.	Substrate	Time, h	Product	Yield, %
1.	$C_6H_5.CO.CH_3$	5	$\alpha C_6H_5.CHOH.CH_3$	97
2.	$4\text{-}CH_3O.C_6H_4.CHO$	5	$4\text{-}CH_3O.C_6H_4.CH_2OH$	80
3.	$C_6H_{10}O$	12	$C_6H_{11}OH$	56
4.	$C_6H_5.CH=CH.COCH_3$	18	$C_6H_5.CH=CH.CH.OH.CH_3$	72
5.	$C_6H_5CH_2CN$	24	NR	NR
6.	$4\text{-}CH_3.C_6H_5SO_2N_3$	5	$4\text{-}CH_3.C_6H_5SO_2NH_2$	97
7.	$4\text{-}CH_3O.C_6H_5.CH = N.C_6H_5$	14	$4\text{–}H_3O.C_6H_5.CH_2NH.C_6H_5$	73
8.	$C_6H_5.CH=CH.CHO$	8	$C_6H_5.CH=CH.CH_2OH$	92
9.	$C_6H_5.CO.COOCH_3$	8	$C_6H_5.CHOH.COOCH_3$	83
10.	$2\text{-}CH_3.C_6H_9O$	12	$Trans\text{-}2\text{-}CH_3.C_6H_{10}OH$	82
11.	$4\text{-}CH_3.C_6H_4.NO_2$	12	$4\text{-}CH_3.C_6H_4.NH_2$	68

Table–3: $Ni\{P(OC_6H_5)_3\}_4$ - Ni (0) catalyzed transfer hydrogenation of aldehydes and ketones using i-C_3H_7OH

S. No.	Substrate	Time, h	Product	Yield %
1.	$C_6H_5.CO.CH_3$	2	$C_6H_5.CHOH.CH_3$	95
2.	4-$CH_3O.C_6H_4.CHO$	8	4-$CH_3O.C_6H_4.CH_2OH$	72
3.	2-$CH_3.C_6H_9O$	24	Trans-2-$CH_3.C_6H_{10}OH$	84
4.	$C_6H_5.CH=CH.COCH_3$	9	$C_6H_5.CH=CH.CH.OH.CH_3$	62
5.	$C_6H_5.CO.CO.C_6H_5$	6	2,3- $C_6H_5.CHOH.CHOH.C_6H_5$	93
6.	4-$CH_3.C_6H_5SO_2N_3$	5	4-$CH_3.C_6H_5SO_2NH_2$	88
7.	4–$CH_3O.C_6H_5.CH=N.C_6H_5$	12	4–$CH_3O.C_6H_5.CH_2NH.C_6H_5$	75
8.	$C_6H_5.CH=CH.CHO$	8	$C_6H_5.CH=CH.CH_2OH$	95
9.	$C_6H_5.CO.COOCH_3$	10	$C_6H_5.CHOH.COOCH_3$	81
10.	$C_9H_{15}CHO$ (Citral)	2	$C_{10}H_{17}OH$	90
11.	$C_9H_{17}CHO$ (Citronellal)	16	$C_{10}H_{19}OH$ (Citronellol)	94

$HCOONH_4$ and isopropyl alcohol were used for the reduction of several ketones and aldehydes in the presence of $Ni\{P(OC_6H_5)_3\}_4$ as catalyst (Table-2, 3). These reductions were also accelerated by the use of NaOH or KOH as co-catalyst. Keto alcohols, keto esters, aromatic and aliphatic ketones, aldehydes α,β-unsaturated aldehydes, ketones were also reduced by this catalyst with isopropyl alcohol. The carbonyl moiety was selectively reduced in the presence of 2-methyl cyclohexanone and benzoin gave the trans isomers as the reduction products. Phenylacetonitrile was not reduced while an imine (4-methoxy benzylidene aniline) could be easily reduced.

The use of ethanol amine with Ru catalysts has been reported to cause reduction of acetophenones at room temperature.[14] Chiral ethanolamines have been used for asymmetric induction in such reactions.[15] In the case of $Ni\{P(OC_6H_5)_3\}_4$ also, the use of

ethanol amine led to reduction of acetophenone and anisaldehyde at room temperature in high yield.

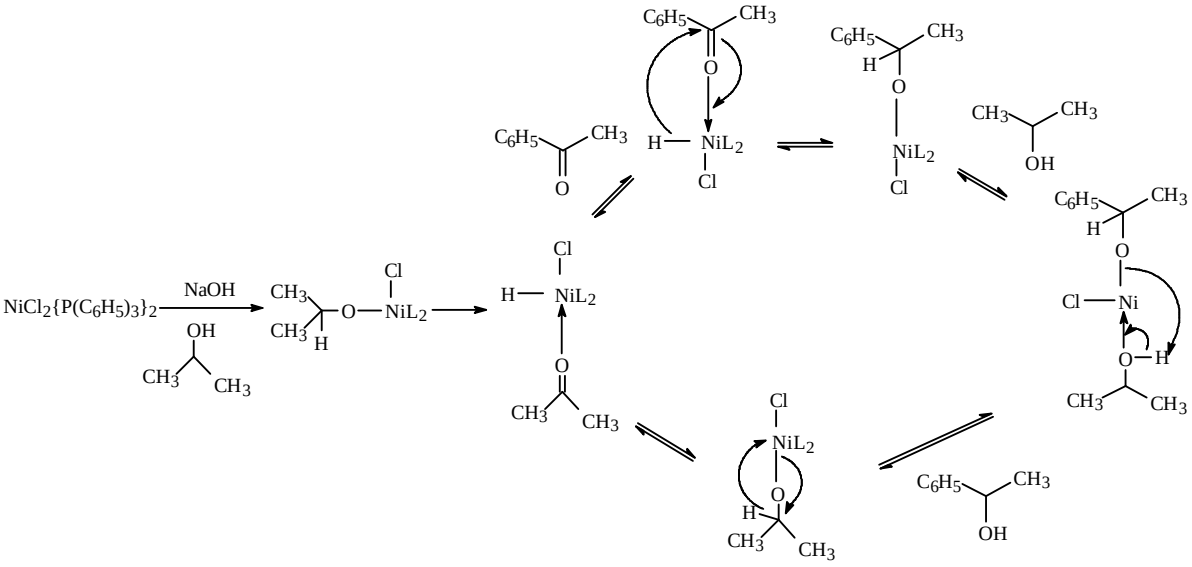
$Ni\{P(OC_6H_5)_3\}_4$ is a better catalyst (faster reactions) than $NiCl_2\{P(C_6H_5)_3\}_2$ and to our best knowledge is the first example of a non halide homogeneous catalyst used for transfer hydrogenation. Acetophenone is completely reduced in 2 h with Ni (0) compared to 30 h with Ni (II) using isopropyl alcohol as reducing agent. Methyl mandelate (10 h vs 36 h), cinnamaldehyde (8 h vs 30 h) also react faster with Ni (0) as catalyst while aliphatic ketones show similar reaction times with both the catalyst. The selective reductions of cinnamaldehyde (cinnamyl alcohol - 95 % in 8 h Vs 51 % in 30 h), citronellal (citronellol - 94 % in 16 h Vs 57 % in 24 h) are also higher yielding, with Ni-(0) compared to Ni-(II). The proposed mechanism of the reaction differs for the two catalysts with what we believe is a preliminary oxidative addition mechanism for the Ni (0) catalyst as compared to a nucleophilic displacement of Cl^- from the Ni (II) complex, both leading to a NiH species.

The mechanism of the reaction is depicted in (*Figure-1*) (i) nucleophilic displacement of the Cl^- by i-$C_3H_7O^-$ (generated by the abstraction of the H from i-C_3H_7OH by the base NaOH/KOH (ii) β-hydride elimination to form a NiH species with elimination of acetone (iii) co-ordination of the FG (functional group) to the Ni species (iv) H- migration to the carbonyl C- followed by (v) co-ordination of i-C_3H_7OH (vi) protonation (hydrogen transfer) of the RFG (reduced functional group) and β-hydride elimination to recycle the NiH catalyst .[13]

$HCOONH_4$ has been used as a reducing agent in the presence of Pd/C for the reduction of several functional groups. $Ni\{P(OC_6H_5)_3\}_4$ forms NiH in the presence of acids and also undergoes oxidative addition to aryl iodides. Ni (0) catalyst could

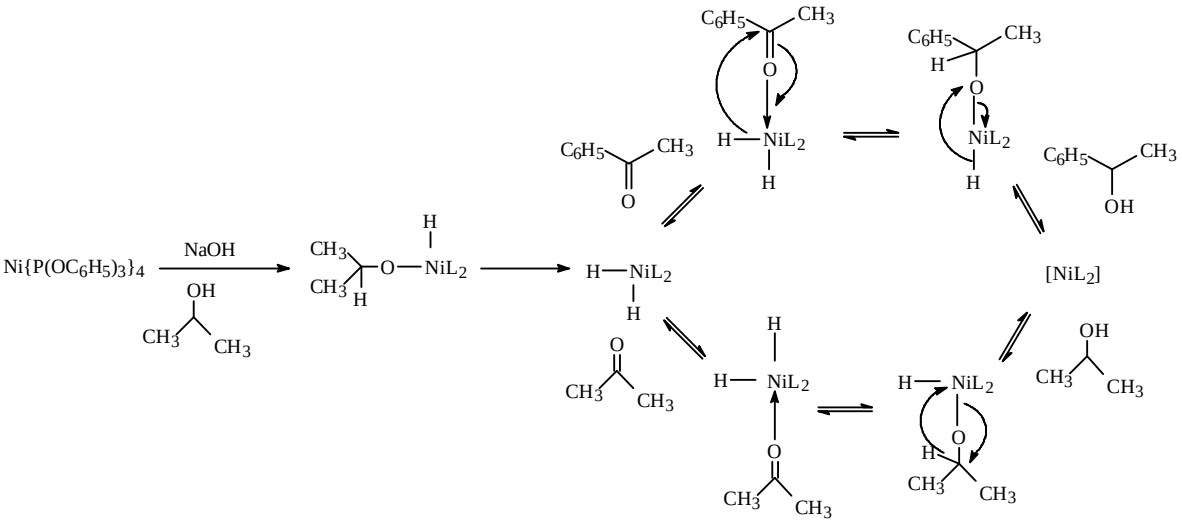
oxidatively add to $HCOONH_4$ forming NiH, which could cause reduction of the different functional groups. A number of aldehydes and ketones were reduced by $HCOONH_4$ in the presence of this catalyst using acetic acid as solvent. Reactions were slower in methanol.

Figure-1: Ni (II) catalyzed transfer hydrogenation – catalytic cycle



The reaction probably proceeds via the following sequence of events (i) oxidative addition of Ni (0) to i -C_3H_7OH to form NiH species (ii) β-hydride elimination leading to acetone and a NiH_2 species (iii) coordination of the FG (Functional Group) to the NiH_2 complex and transfer of H to the coordinating FG (iv) reductive elimination of the RFG (Reduced Functional Group) by transfer of the remaining H to the coordinating FG and recycling of the catalyst .[13] The catalytic cycle is depicted in *Figure-2*

Figure-2: Ni{P(OC$_6$H$_5$)$_3$}$_4$-Ni (0) Catalyzed transfer hydrogenation – catalytic cycle



Preliminary studies on the asymmetric reduction of acetophenone with isopropyl alcohol using Ni{P(OC$_6$H$_5$)$_3$}$_4$ as catalyst using chiral ligands like DIOP, l-proline, methionine, glucosamine, phenyl glycine, threonine, alanine, ephedrine gave low ee of the reduction product. The ligands were added as additives. A solution of acetophenone, KOH, catalyst and the chiral ligand were refluxed in isopropanol for 5 - 24 h. The reactions were incomplete and the product was purified in the usual manner. Optical rotation was measured on a Jasco digital polarimeter in a cell of 0.5 dm length and 1 ml volume. Solution of the acetophenone in methanol of concentration 3.0 g in 100 ml was prepared for these measurements and compared with the known value of (+)-42 / (-)-42 (c = 3, CH_3OH).

Phenyl glycine was expected to give high asymmetric induction due to its similarity in structure to the product 1-phenyl ethanol. The transfer hydrogenation in

presence of R-(-)-phenyl glycine gave R-(+)-phenyl ethanol with $[\alpha]^{28}_{D}$ (+)-1.6 (Rotation – (+) 0.024) and enantioselectivity (ee) of only 3.8%. S-(-)-proline gave the opposite stereochemistry S-(-)-phenethanol $[\alpha]^{28}_{D}$

(-)-1.43 and enantioselectivity (ee) of 3.4 %. L-Diethyl tartarate and L-threonine gave (R)-(+)-phenethanol of $[\alpha]^{28}_{D}$ (+)-1.25 and $[\alpha]^{28}_{D}$ (+)-3.0 and enantioselectivity (ee) of 3.0 and 7.14 %. The asymmetric induction with all these ligands were low (Table-4)

Table-4 : $Ni\{P(OC_6H_5)_3\}_4$ - Ni (0) - catalyzed asymmetric transfer hydrogenation of acetophenone with i-C_3H_7OH

S. No.	Chiral Ligand	Time, h	Specific Rotation $[\alpha]^{28}_{D}$	ee %
1.	R-(-)-Phenyl glycine	5.5	(+)-0.024	3.8
2.	S-(-)-Proline	2.5	(-)-1.43	3.4
3.	L-Diethyltartarate	6	(+)-1.25	3
4.	L-Threonine	16	(+)-3	7.14
5.	Racemic-Phenylglycine	10	(+)-2.0	4.7
6.	Racemic-Phenylglycinol	24	(+)-0.706	2.68
7.	Racemic-Phenylglycine[a]	18	(+)-0.56	1.3
8.	Racemic-Phenylglycine[b]	24	(-)-0.86	2.04
9.	R-(-)-Phenylglycine[a]	24	(-)-1.33	3.16
10.	S-(+)-Phenylglycine[a]	24	(+)-1.6	3.80

a : Catalyst – $RuCl_2(DMSO)_4$ b : $RuCl_2\{P(C_6H_5)_3\}_3$

Racemic ligands with a slight excess of one enantiomer have been show to cause high asymmetric induction.[16] Selective formation of diastereomeric transition metal intermediates could probably cause asymmetric induction in transfer hydrogenations using racemic ligands. Based on this hypothesis, the reduction of acetophenone using

$Ni\{P(OC_6H_5)_3\}_4$, Ni (0) catalyst and isopropanol, with racemic phenyl glycine and phenyl glycinol as ligand additives gave R-(+)-1-phenethanol $[\alpha]^{28}_D$ (+)-2.0 and (+)-0.706 with a low enantioselectivity of 4.7 and 2.68 %, comparable to the results obtained with the chiral ligands. This is the first observation of asymmetric transfer hydrogenation using racemic ligands.

We have reported the use of $RuCl_2(DMSO)_4$ and other complexes as efficient transfer hydrogenation catalysts.[17] The influence of racemic ligands was also demonstrated in $RuCl_2(DMSO)_4$ and $RuCl_2\{P(C_6H_5)_3\}_3$ catalyzed transfer hydrogenation of acetophenone. Racemic phenyl glycine and $RuCl_2(DMSO)_4$ gave (+)-phenethyl alcohol with 1.3% enantiomeric excess. R-(-)-phenyl glycine gave S-(-)-phenethyl alcohol, ee 3.16% while the S-(+)-phenyl glycine gave (+)-phenethyl alcohol with 3.80% ee. $RuCl_2\{P(C_6H_5)_3\}_3$ with racemic phenyl glycine gave S-(-)-phenethyl alcohol with 2.04% ee. This supports our hypothesis of racemic ligands forming selective diastereomeric intermediates which cause stereoselective reduction of the acetophenone.

Both $Ni\{P(OC_6H_5)_3\}_4$ and $RuCl_2(DMSO)_4$ with racemic phenyl glycine and phenyl glycinol gave the R-(+)-phenethyl alcohol in enantiomeric excesses of 1.3 – 4.7%. In comparison $RuCl_2\{P(C_6H_5)_3\}_3$ gave the opposite enantiomeric S-(-)-phenethyl alcohol. The optical induction observed with the racemic ligands in comparable to that obtained with the chiral ligands, both R- and S- isomers.

The transfer hydrogenation of ketones and aldehydes using isopropyl alcohol was catalyzed by (Ni-II) $NiCl_2\{P(C_6H_5)_3\}_2$ and (Ni-0) $Ni\{P(OC_6H_5)_3\}_4$ with NaOH/KOH as co-catalyst. $HCOONH_4$ and iso-propanol were efficient reducing agents in the presence of these Ni catalysts. $Ni\{P(OC_6H_5)_3\}_4$ is the first example of a non halide transition

metal catalyst for transfer hydrogenation and a different initiation of the hydrogenation process is used. Racemic ligands have been shown to cause asymmetric transfer hydrogenation of acetophenone with low enantioselectivity. Further work is in progress on the design, use of racemic ligands, metal complexes and mechanism of the transfer hydrogenation reaction.

Table-5 : $Ni\{P(OC_6H_5)_3\}_4$ - Ni (0) and Ru (II) - catalyzed asymmetric transfer hydrogenation of acetophenone with i-C_3H_7OH

S. No.	Chiral Ligand	Time, h	Specific Rotation $[\alpha]^{28}_D$	ee %
1.	Ephedrine[a]	24	-(1.28)	3.07%
2.	Diethyl tartarate[a]	24	+(1.25)	3.00%
3.	glucose[a]	48	No Rotation	
4.	Glucose amine[a]	24	No Rotation	
5.	R(-)-phenylglycine[a,d]	48	No Rotation	
6.	Racemic phenyl glycine[c]	24	+(1.32)	3.14%
7.	Racemic phenyl glycine[b]	18	+1.41	3.35%
8.	R(-)-phenyl glycine[b]	24	-(1.33)	3.16%
9.	S(+)-phenyl glycine[b]	24	+1.6	3.80%
10.	Racemic phenyl glycine[a]	24	No Rotation	
11.	R(-) phenyl glycine[a]	12	No Rotation	
12.	R(-) phenyl glycine[a,f]	24	No Rotation	
13.	DIOP[a]	48	No Rotation	

a: Catalyst – $Ni\{P(OC_6H_5)_3\}_4$ b: $RuCl_2$ $(DMSO)_4$
c: $RuCl_2$ $\{P(C_6H_5)_3\}_3$ d: Solvent Triethylamine / formic acid
e: $RuCl_2$ (COD) f: $SoCl_2$ / ethylene glycol

Asymmetric transfer hydrogenations of actophenone were done chiral ,achiral and racemic ligands as listed in Table-4 and Table-5 with $Ni\{P(OC_6H_5)_3\}4$, $RuCl_2$ $(DMSO)_4$

and $RuCl_2\{P(C_6H_5)_3\}_3$ catalysts in isopropanol as solvent and KOH as co-catalysts to get phenethyl acohol with comparable enantioselectivity.

Ephedrine, glucose, glucoseamine, diethyltartarate, R(-)phenylglycinol, R(-) phenylglycine and racemic phenylglycine were used as chiral ligands.

Reactions were also carried out using formic acid and triethylamine in the ratio of (5:2).However the transfer hydrogenation of acetophenone using R (-) phenylglycine did not go to completion even after 48 h of reflux.

Acetophenone was reduced to R (-)–1-phenethanol $[\ \alpha\ ]^{28}_D$ (-1.28) enantioselectivity of 5.42% when ephedrine (1mm,0.165g) was used as the chiral ligand for the reaction of acetophenone (3mm) to phenethylaclcohol using catalyst Ni $\{P(OC_6H_5)_3\}_4$ (0.1g) and KOH (025mm) as co-catalyst stirred at room temperature in isopropanol for 24 h

When Diethytartarate (0.040 g) was used as the chiral ligand R-(+) phenethanol of $[\ \alpha\ ]^{28}_D$ (+) (1.25) and 3% of ee was obtained in 6 h with Ni (0) catalyst (0.062) and KOH (0.056 g) used as the co-catalyst and isopropanol as solvent.

There was however no reaction of transfer hydrogeantion of actophenone and no specific rotation when glucose (0.090g, 5mm) was used as the chiral ligand even after 24 h of reflux in isopropanol as the solvent and KOH as the co-catalyst.

Glucoseamine $[\ \alpha\ ]^{26}_D$ (+) 82.4 (0.1 mm) was used in view of the finding of Noyori that ethanolamine and ethylene diamine catalyze the ruthenium catalyzed transfer hydrogenation reactions at room temperature ,so we tried $RuCl_2$ ($DMSO)_4$ and $Ru\ \{P(C_6H_5)\}_3$ catalyzed transfer hydrogenation with glucoseamine as chiral ligand. However under the conditions studied no reaction was observed for the transfer

hydrogenation of acetophenone even after 24 h of reflux in isopropanol as solvent and KOH (0.020 g) as co-catalyst.

Transfer hydrogenation of acetophenone (5 mm) was carried out with racemic phenylglycine (0.10 mm) and $RuCl_2\{P(C_6H_5)_3\}_3$ (0.01mm) NaOH (0.009g) and isopropanol reflux for 24 h afforded $[\alpha]^{28}_D$ +(1.32) and 3.14 % ee.

Enantioselectivity of 3.35% and $[\alpha]^{28}_D$ of +1.41 was obtained with reaction of racemic phenylglycine (0.10mm) and Ru Cl_2 $(DMSO)_4$ catalyst (0.01mm) in isoprooanol at refux for 18 h and KOH as co-catalyst and acetophenone as the sustrate (3mm).

However no reaction and enantioselectivity of the transfer hydrogenation of acetophenone was observed with $RuCl_2$ (COD) (0.010 g) as catalyst and KOH (0.004 mm) as co-catalyst in isopropanol.

Thus in comparison with Ni (0) and Ru (II) catalysts RuCl2 (DMSO)4 catalyst gave comparable enantioselectivities with chiral and racemic ligands ranging from 1.3% ee to 4.7% ee.The optical rotation observed with racememic ligands is comparable to that obtained with chiral ligands ,both R and S isomers. Racemic ligands re thus shown to cause asymmetric induction in the transfer hydrogenation of acetophenone with low enantioselectivity.

Experimental

$NiCl_2\{P(C_6H_5)_3\}_2$ and $Ni\{P(OC_6H_5)_3\}_4$ were prepared according to the literature procedure.[17] The isopropyl alcohol reactions were carried out under Ar atmosphere. The aldehydes, ketones chiral ligands are commercially available (Aldrich, Loba Chemie, Sd Fine Chemicals) or synthesized by known methods and the reduced products were characterized by IR, ^1H NMR and MS.[18] Optical rotations were measured on a Jasco digital polarimeter using a polarimeter cell of 0.5 dm length in methanol. Silica gel (100 – 200 mesh) was used for column chromatography.

1. $NiCl_2(PPh_3)_2$ catalyzed transfer hydrogenation of acetophenone using isopropyl alcohol

A solution of acetophenone (0.6 g, 5 mmol) $Ni\{P(OC_6H_5)_3\}_4$ (0.130 g, 0.1 mmol), KOH (0.01 g, 0.178 mmol), Racemic-phenylglycine (0.04 g, 0.265 mmol) in isopropyl alcohol (10 ml) was refluxed for 2 hr to give after the usual workup and purification ®-(+)-1-phenylethanol with 4.7% ee (0.245 g, 40%, recovered acetophenone – 0.120 g, 20%, Rotation – (+)-0.024, $[\alpha]^{28}_D$: 2.0, Enantiomeric excess (ee) – 4.7% c – 0.030 g in 1 ml methanol). A 3% (0.03 g in 1 ml methanol) solution of 1-phenethanol in methanol was prepared and used for optical rotation measurements. The observed rotation was +2.0 (compared to the known value of +42, c = 3.0 in CH_3OH).

2. $NiCl_2\{P(C_6H_5)_3\}_2$ catalyzed selective transfer hydrogenation of cinnamaldehyde using isopropyl alcohol

A solution of acetophenone (0.6 g, 5 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.130 g, 0.1 mmol), KOH (0.01 g, 0.178 mmol), Racemic-phenylglycinol (0.04 g, 0.29 mmol) in isopropyl alcohol (10 ml) was refluxed for 24 hr to give after the usual workup and purification R-(+)-1-phenylethanol with 2.68 % ee (0.069 g, 11% recovered acetophenone – 0.391 g, 65% Rotation – (+)-0.01, $[\alpha]^{28}_D$: 0.706, Enantiomeric excess (ee) – 2.68%, c – 0.030 g in 1 ml methanol). A 3% (0.03 g in 1 ml methanol) solution of the 1-phenethanol in methanol was prepared and used for optical rotation measurements. The observed rotation was +0.01 (compared to the known value of +42, c = 3.0 in CH_3OH)

3. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed asymmetric transfer hydrogenation of acetophenone using isopropyl alcohol with R (-) Phenylglycine

A solution of acetophenone (0.6 g, 5 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.062 g, 0.05 mmol), KOH (0.056 g, 1 mmol), R-(-)-phenylglycine (0.072 g, 0.5 mmol) in isopropyl alcohol (10 ml) was refluxed for 5.5 hr to give after the usual workup and purification ®-(+)-1-phenylethanol with 3.8% enantiomeric excess (0.177 g, 29%, recovered acetophenone – 0.300 g, 50%, optical rotation – (+) 0.024, $[\alpha]^{28}_D$: (+)-1.6, c – 0.030 g in 1 ml methanol). A 3% (0.03 g in 1 ml methanol) solution of 1-phenethanol in methanol was prepared and used for optical rotation measurements. The observed

rotation was (+)-0.024 (compared to the known value of +42, c = 3.0 in CH_3OH) with $[\alpha]^{28}_D$: +1.6 and ee of 3.8%.

4. $RuCl_2(DMSO)_4$ catalyzed asymmetric transfer hydrogenation of acetophenone using isopropyl alcohol with racemic phenylglycine

A solution of acetophenone (0.60 g, 5 mmol), $RuCl_2(DMSO)_4$ (0.012 g, 0.05 mmol), KOH (0.014 g, 0.25 mmol), Racemic-phenylglycine (0.0137 g, 0.1 mmol) in isopropyl alcohol (10 ml) was refluxed for 18 hr to give after the usual workup and purification (R)-(+)-1-phenylethanol with 1.3 % ee (0.486 g, 81%, recovered acetophenone – 0.028 g, 4.7%, Rotation – (+)-0.0085, $[\alpha]^{28}_D$: 0.56, Enantiomeric excess – 1.3 %, c – 0.030 g in 1 ml methanol). A 3% (0.03 g in 1 ml methanol) solution of 1-phenethanol in methanol was prepared and used for optical rotation measurements. The observed rotation was (+)-0.0085 (compared to the known value of +42, c = 3.0 in CH_3OH).

5. $RuCl_2(DMSO)_4$ catalyzed asymmetric transfer hydrogenation of acetophenone using isopropyl alcohol with (-(-)-phenylglycine

A solution of acetophenone (0.60 g, 5 mmol), $RuCl_2(DMSO)_4$ (0.012 g, 0.05 mmol), KOH (0.014 g, 0.25 mmol), R-(-)-phenylglycine (0.0137 g, 0.1 mmol) in isopropyl alcohol (10 ml) was refluxed for 24 hr to give after the usual workup and purification R-(-)-1-phenylethanol with 3.16% ee (0.488 g, 80%, recovered acetophenone – 0.120 g, 20%, Rotation – (+)-0.020, $[\alpha]^{28}_D$: 1.33, Enantiomeric excess

– 3.16%, c – 0.030 g in 1 ml methanol). A 3% (0.03 g in 1 ml methanol) solution of 1-phenethanol in methanol was prepared and used for optical rotation measurements. The observed rotation was (+)-0.020 (compared to the known value of (-)-42, c = 3.0 in CH_3OH).

6. $RuCl_2\{P(C_6H_5)_3\}_3$ catalyzed asymmetric transfer hydrogenation of acetophenone using isopropyl alcohol with Racemic phenylglycine

$RuCl_2\{P(C_6H_5)_3\}_3$ (0.010 g, 0.05 mmol) was refluxed in isopropanol (5 ml) under Ar for 10 minutes, a degassed solution of acetophenone (0.60 g, 5 mmol) in isopropanol (10 ml) was added dropwise to the reaction solution. The resulting gray solution was stirred for 10 minutes and then a solution of NaOH (0.009 g, 0.22 mmol) was added to form a homogeneous solution. Racemic phenylglycine (0.04 g, 0.029 mmol) was added to the reaction mixture and refluxed for 24 hr to give after the usual workup and purification (R)-(-)-1-phenylethanol with 2.04% ee (0.074 g, 12 %, recovered acetophenone – 0.420 g, 70%, Rotation – (-)-0.013, $[\alpha]^{28}_D$: 0.86, Enantiomeric excess – 2.04%, c – 0.030 g in 1 ml methanol). A 3% (0.03 g in 1 ml methanol) solution of 1-phenethanol in methanol was prepared and used for optical rotation measurements. The observed rotation was (-)-0.013 (compared to the known value of (-)-42, c = 3.0 in CH_3OH).

7. $Ni\{P(OC_6H_5)_3\}_2$ catalyzed transfer hydrogenation of acetophenone using isopropyl alcohol

A solution of acetophenone (0.360 g, 3 mmol) in isopropyl alcohol (10 ml) containing $NiCl_2\{P(C_6H_5)_3\}_2$ (0.354 g, 15 mol %, 0.45 mmol) and NaOH (0.04 g, 1 mmol) was refluxed for 30 hr and monitored by TLC. After completion, the reaction mixture was concentrated on a rotary evaporator, extracted with ethyl acetate and washed with dilute HCl (3 x 25 ml), brine, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography over silica gel to give α-phenethyl alcohol (0.300 g, 82%)..

BP : 83 - 84°C / 9 mm of Hg.

IR (cm^{-1}) 3320, 2980, 2940, 2900, 2800, 2460, 1960, 1895, 1615, 1505, 1460, 1380, 1225, 1070, 1020, 910, 750

^{1}H-NMR (δ, $CDCl_3$, 80 MHz), 7.23 (m, 5H, Ar), 4.83 – 4.5 (q, 8Hz, 1H, C<u>H</u>.CH_3), 4.0 (s, 1H, O<u>H</u>), 1.3 – 1.2 (d, 8Hz, 3H, CH.C<u>H</u>$_3$).

8. $NiCl_2\{P(C_6H_5)_3\}_2$ catalyzed selective hydrogenation of cinnamaldehyde using isopropyl alcohol

A solution of cinnamaldehyde (0.396 g, 3 mmol) in isopropyl alcohol (10 ml) containing $NiCl_2\{P(C_6H_5)_3\}_2$ (0.130 g, 0.2 mmol) and NaOH (0.3 g, 0.75 mmol) was refluxed for 24 hr and monitored by TLC. After completion, the reaction mixture was concentrated on a rotary evaporator, extracted with ethyl acetate and washed with 10%

HCl (3 x 25 ml), brine, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography over silica gel to give cinnamyl alcohol (0.205 g, 51%).

BP : 250 °C

IR (cm^{-1}): 3450, 3010, 2850, 1600, 1500, 1450, 1200, 1085, 1060, 1010, 960, 740, 690

^{1}H-NMR (δ, $CDCl_3$, 80 MHz): 7.2 (m, 5H, Ar), 6.8 – 6.11 (m, 2H, CH=CH), 4.23 (d, 2H, CH_2), 1.68 (bs, 1H, OH).

9. $NiCl_2\{P(C_6H_5)_3\}_2$ catalyzed transfer hydrogenation of benzoylmethylformate using isopropyl alcohol

A solution of benzoylmethylformate (0.492 g, 3 mmol) in isopropyl alcohol (10 ml) containing $NiCl_2\{P(C_6H_5)_3\}_2$ (0.130 g, 0.2 mmol) and NaOH (0.03 g, 0.75 mmol) was refluxed for 24 hr and monitored by TLC. After completion, the reaction mixture was concentrated on a rotary evaporator, extracted with ethyl acetate and washed with 10% HCl (3 x 25 ml), brine, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography over silica gel to give methylmandelate (0.329 g, 66%).

BP : 135 °C/12mm of Hg

IR (cm^{-1}): 3520, 3030, 2970, 1745, 1610, 1505, 1450, 1300, 1230, 1100, 1080, 760, 680

^{1}H-NMR (δ $CDCl_3$, 90 MHz): 7.29 (bs, 5H, Ar), 5.13 (d, 1H, C_6H_5.CH), 3.69 (s, 3H, $COOCH_3$), 3.42 (d, 1H, OH); MS (m/z) 166 (M^+ - 3), 107 (92), 89 (3), 79 (91), 77 (100), 74 (4), 63 (6), 59 (5), 51 (60).

10. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of benzoylmethyl formate using ammonium formate

A solution of benzoylmethylformate (0.328 g, 2 mmol), ammonium formate (1.513 g, 24 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.1 g, 0.077 mmol) was refluxed in acetic acid (10 ml) for 8 hr. The reaction mixture was monitored by TLC and after completion, concentrated on a rotary evaporator, neutralized with saturated $NaHCO_3$, extracted with ethylacetate, the combined organic extracts washed with water, brine, dried over anhydrous Na_2SO_4 concentrated and purified by column chromatography over silica gel (100 – 200 mesh) to give methylmandelate (0.284 g, 83 %).

11. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of 4-phenylbut-3-en-2-one using ammonium formate

A solution of 4-phenylbut-3-en-2-one (0.438 g, 24 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.1 g, 0.077 mmol) was refluxed in acetic acid (10 ml) for 18 hr. The reaction mixture was monitored by TLC and after completion, concentrated on a rotary evaporator, neutralized with saturated $NaHCO_3$, extracted with ethylacetate, the combined organic extracts washed with water, brine, dried over anhydrous Na_2SO_4 concentrated and purified by column chromatography over silica gel (100 – 200 mesh) to give 4-phenylbut-3-en-2-ol (0.404 g, 81%)

IR (cm^{-1}) 3310, 3010, 2985, 1450, 1370, 1140, 1060, 760, 700, 540, 390

^{1}H-NMR (δ $CDCl_3$, 200 MHz): 7.5 – 7.25 (m, 5H, Ar), 6.64 – 6.57 (d, 14 Hz, 1H, C_6H_5.CH=), 6.34 – 6.24 (dd, 14, 6 Hz, 1H, =CH.CHOH), 4.6 – 4.45 (m, 1H, CH.OH), 1.9 (bs, 1H, OH), 1.42 – 1.39 (d, 6 Hz, 3H, CH.CH_3).

12. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of cinnamaldehyde using ammonium formate

A solution of cinnamaldehyde (0.396 g, 3 mmol), ammonium formate (1.513 g, 24 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.1 g, 0.077 mmol) was refluxed in acetic acid (10 ml) for 8 hr. The reaction mixture was monitored by TLC and after completion, concentrated on a rotary evaporator, neutralized with saturated $NaHCO_3$, extracted with ethylacetate, the combined organic extracts washed with water, brine, dried over anhydrous Na_2SO_4 concentrated and purified by column chromatography over silica gel (100 – 200 mesh) to give cinnamyl alcohol (0.370 g, 92%).

13. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of benzoin using ammonium formate

A solution of benzoin (0.636 g, 3 mmol), ammonium formate (1.513 g, 24 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.1 g, 0.077 mmol) was refluxed in acetic acid (10 ml) for 5 hr. The reaction mixture was monitored by TLC and after completion, concentrated on a rotary evaporator, neutralized with saturated $NaHCO_3$, extracted with ethylacetate, the combined organic extracts washed with water, brine, dried over anhydrous Na_2SO_4

concentrated and purified by column chromatography over silica gel (100 – 200 mesh) to give diphenylethyleneglycol (0.497 g, 72%).

IR (cm^{-1}): 3300, 1450, 1380, 1020, 700, 500, 370

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 7.4 – 7.1 (m, 10 H, Ar), 4.85 (s, 2 H, $C_6H_5.CH$, major, erythro), 4.72 (s, 2 H, $C_6H_5.CH$, minor, threo, ratio – 10 : 1.8), H), 2.95 (bs, 2 H, CH.OH, minor), 2.32 (bs, 2 H, CH.OH, major, ratio – 10 : 1.2).

14. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of 4-toluene sulfonylazide using ammonium formate

A solution of 4-toluenesulfonylazide (0.551 g, 3 mmol), ammonium formate (1.513 g, 24 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.1 g, 0.077 mmol) was refluxed in acetic acid (10 ml) for 24 hr. The reaction mixture was monitored by TLC and after completion, concentrated on a rotary evaporator, neutralized with saturated $NaHCO_3$, extracted with ethylacetate, the combined organic extracts washed with water, brine, dried over anhydrous Na_2SO_4 concentrated to give a mixture of $4\text{-}CH_3.C_6H_4.SO_2NH_2$ (0.500 g, 97%).

IR (cm^{-1}): 3310, 3240, 2960, 2920, 2860, 1580, 1460, 1380, 1330, 1160, 1100, 910, 820, 710, 680

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 7.65 – 7.60 (d, 10 Hz, 2 H, C_6H_4), 7.12 – 7.07 (d, 10 Hz, 2 H, C_6H_4), 6.23 (bs, 2 H, NH_2), 2.25 (s, 3 H, CH_3).

15. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of 4-nitrotoluene using ammonium formate

A solution of 4-nitrotoluene (0.411 g, 3 mmol), ammonium formate (1.513 g, 24 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.1 g, 0.077 mmol) was refluxed in acetic acid (10 ml) for 24 hr. The reaction mixture was monitored by TLC and after completion, concentrated on a rotary evaporator, neutralized with saturated $NaHCO_3$, extracted with ethylacetate, the combined organic extracts, washed with water, brine, dried over anhydrous Na_2SO_4 concentrated to give a mixture of 4-toluidine (0.220 g, 68.5 %) and recovered starting material (0.130 g, 30 %).

IR (cm^{-1}): 3300, 3200, 2800, 2820, 1610, 1500, 1450, 1370, 1180, 1110, 1030, 810, 500

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 7.07 – 7.01 (d, 12 Hz, 2 H, $C_6\underline{H}_4$), 6.68 – 6.62 (d, 12 Hz, 2 H, $C_6\underline{H}_4$), 3.60 (bs, 2 H, $N\underline{H}_2$), 2.32 (s, 3 H, $C\underline{H}_3$).

16. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of N-phenyl-4-methoxybenzaldimine using ammonium formate

A solution of N-phenyl-4-methoxybenzaldimine (0.422 g, 2 mmol), ammonium formate (1.513 g, 24 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.1 g, 0.077 mmol) was refluxed in methanol (10 ml) for 20 hr. The reaction mixture was monitored by TLC and after completion, concentrated on a rotary evaporator, neutralized with saturated $NaHCO_3$, extracted with ethylacetate, the combined organic extracts washed with water, brine, dried over anhydrous Na_2SO_4 concentrated to give a mixture of N-phenyl-4-methoxybenzyl amine (0.308 g, 72%).

IR (cm^{-1}) 3300, 1590, 1490, 1450, 1230, 1160, 1010, 750, 690, 530

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 8.5 (s, 1 H, NH), 7.45 – 7.01 (m, 7 H, Ar), 6.85 – 6.77 (d, 16 Hz, 2 H, C_6H_4), 4.92 (s, 2 H, CH_2), 3.72 (s, 3 H, OCH_3).

17. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of citral using isopropyl alcohol

A solution of citral (0.304 g, 2 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.1 g, 0.077 mmol), KOH (0.02 g, 0.36 mmol) was refluxed in isopropyl alcohol (10 ml) for 2 hr. and monitored by TLC. After completion of the reaction, the reaction mixture was concentrated on a rotary evaporator, extracted with ethyl acetate and washed with 10% HCl (3 x 25 ml), brine, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography over silica gel to give geraniol (0.280 g, 91%).

IR (cm^{-1}): 3300, 2800, 1430, 1370, 1050, 1000

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 5.45 – 5.32 (t, 6 Hz, 1 H, C=CH.CH_2), 5.15 – 5.05 (t, 6 Hz, 2 H, C=CH.CH_2), 4.16 – 4.13 (d, 6 Hz, 2 H, CH_2.OH), 1.60 (s, 6 Hz, C=C(CH_3)$_2$), 1.50 – 1.05 (m, 4 H, CH.CH_2.CH_2.C=), 0.90 – 0.87 (s, 6 Hz, 3 H, C.CH_3).

18. $Ni\{P(OC_6H_5)_3\}_4$ catalyzed transfer hydrogenation of citronellal using isopropyl alcohol

A solution of citronellal (0.304 g, 2 mmol), $Ni\{P(OC_6H_5)_3\}_4$ (0.1 g, 0.077 mmol), KOH (0.02 g, 0.36 mmol), was refluxed in isopropyl alcohol (10 ml) for 16 hr and monitored by TLC. After completion, the reaction mixture was concentrated on a rotary

evaporator, extracted with ethyl acetate and washed with 10% HCl (3 x 25 ml), brine, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography over silica gel to give geraniol (0.294 g, 94%).

IR (cm^{-1}): 3200, 2800, 1650, 1390, 1320, 1000, 450

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 5.15 – 5.05 (m, 1 H, C=C<u>H</u>.CH_2), 3.72 – 3.60 (m, 2 H, C<u>H</u>$_2$OH), 2 (m, 2 H, C<u>H</u>$_2$), 1.68 (s, 3 H, C<u>H</u>$_3$), 1.58 (s, 3 H, C<u>H</u>$_3$), 1.40 – 1.1 (m, 4 H, C.C<u>H</u>$_2$.C<u>H</u>$_2$.C), 0.9 – 0.8 (m, 4 H, =C.C<u>H</u>$_3$ and C<u>H</u>.$(CH_3)_2$).

19. Ni{P(OC_6H_5)$_3$}$_4$ catalyzed transfer hydrogenation of tetralone using isopropyl alcohol with ethanol amine as ligand

A solution of tetralone (0.292 g, 2 mmol), Ni{P(OC_6H_5)$_3$}$_4$ (0.1 g, 0.077 mmol), KOH (0.02 g, 0.36 mmol), ethanol amine (0.061g, 1 mmol) was stirred at room temperature in isopropyl alcohol (10 ml) for 16 hr and monitored by TLC. After completion, the reaction mixture was concentrated on a rotary evaporator, extracted with ethyl acetate and washed with 10% HCl (3 x 25 ml), brine, dried over anhydrous Na_2SO_4, concentrated and purified by column chromatography over silica gel to give 1,2,3,4-tetrahydro-1-naphthol (0.284 g, 95%).

20. Ni{P(OC_6H_5)$_3$}$_4$ catalyzed transfer hydrogenation of acetophenone using isopropyl alcohol

A solution of acetophenone (0.240 g, 2 mmol), Ni{P(OC_6H_5)$_3$}$_4$ (0.100 g, 0.077 mmol), KOH (0.02 g, 0.36 mmol), was refluxed in isopropyl alcohol (10 ml) for 1 hr.

After completion, the reaction mixture was concentrated on a rotary evaporator, diluted with 10% HCl, extracted with ethyl acetate, the ethyl acetate extracts concentrated to give α-phenethyl alcohol (0.238 g, 98%).

Conclusion

Thus $Ni\{P(OC_6H_5)_3\}$ is the most efficient and better catalyst than $NiCl_2\{P(C_6H_5)_3\}_2$ and is the first example of a non-halide homogenous catalyst used for transfer hydrogenation, which selectively reduces the carbonyl moiety, keto alcohols, keto esters, aromatic and aliphatic ketones, aldehydes and α,β-unsaturated aldehydes and ketones.

The first use of racemic ligands phenyl glycine and phenyl glycinal with $Ni\{P(OC_6H_5)_3\}_4$ as catalyst was observed to give asymmetric induction of 4.7 and 2.68% ee, for the transfer hydrogenation of acetophenone Ru complexes also gave low asymmetric inductions with both racemic phenyl glycine and R and S phenyl glycine as ligands confirming a hypothesis of selective formation of diastereomeric metal complex intermediates.

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