SYNTHESIS OF CHIRAL FERROCENYLPHOSPHINE

COMPLEXES OF RHODIUM(I) AND THEIR USE

AS CATALYSTS FOR HOMOGENEOUS ASYMMETRIC HYDROGENATION

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ABSTRACT

The present work was directed toward the synthesis of a new chiral catalyst for asymmetric homogeneous hydrogenation. Efficient ways to synthesize the ferrocenylphosphine ligands (R,S)- and (S,R)-α-[2-diphenylphosphinoferrocenyl]ethyldimethylamine ((R,S)- and (S,R)-FcNP) and their cationic rhodium complexes [(diene)Rh($\overset{+}{-}$)FcNP]$^+$A$^-$ were developed. Structural data for the ligand and models of its metal complex have been used to rationalize the stereochemical approach of the substrate to the metal complex, and hence predict the absolute configuration of the product.

The rate of catalytic hydrogenation is dependent on the substrate as is the optical yield of the product alkane. High optical yields are obtained when α-acetamidocinnamic acid is hydrogenated at 1 atm H$_2$ and 32°.

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ABBREVIATIONS

Acac	acetylacetonate
ACMP	o-anisylcyclohexylmethylphosphine
atm	atmosphere
BPPFA	α-1',2-bis(diphenylphosphinoferrocenyl)ethyl-dimethylamine
COD	1,5-cyclooctadiene
DIOP	2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis-(diphenylphosphino)butane
DOPA	3-(3,4-dihydroxyphenyl)-alanine
e.e.	enantiomeric excess
FcN	racemic mixture of N,N-dimethyl-α-ferrocenyl-ethylamine
($\pm$)-FcN	optically active FcN
FcNLi	unisolated lithiated product of FcN, which also is the precursor of FcNP
FcNP	racemic mixture of α-(2-diphenylphosphino-ferrocenyl)ethyldimethylamine
($\pm$)-FcNP	optically active FcNP
IR	infrared
M	molar
NBD	norbornadiene (C_7H_8)
NMDPP	neomenthyldiphenylphosphine
NMR	nuclear magnetic resonance
ppm	parts per million
THF	tetrahydrofuran
TMS	tetramethyl silane

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INTRODUCTION

General Review

The search for and creation of a system which can pro-
duce optical activity in chemical compounds has long been a
goal of the preparative chemist, since the deliberate pro-
duction of asymmetry is an important problem from both the
theoretical and practical point of view. In the case of many
compounds it is only one enantiomer which is useful in bio-
logical systems, and examples are found, for example, in
pharmaceuticals (1), food additives (2), and perfumes (3).
In 1848, Pasteur (4) first succeeded in separating the two
enantiomeric forms of sodium ammonium tartarate with the aid
of forceps and a magnifing lens which initiated much effort
in developing methods of chiral synthesis. Most early results
showed either low optical yield or the need for large quan-
tities of optically active reagents (5,6), consequently many
chemists transfered their attention to biological systems
involving enzymes (7); for only enzymes could convert opti-
cally inactive substances into optically active compounds in
practically 100% optical purity without the help of large
quantities of optically active reagents (7).

In 1956, Akabori, Sakurai, Izumi and Fujii, succeeded in
the asymmetric hydrogenation of various oxime and oxazolone
deriatives; optical yields of up to 35% were obtained. They
used a heterogeneous catalyst consisting of metallic palladium

drawn out on silk (8). The optical purity of the product was found to be dependent on the origin of the silk fibroin and its chemical pretreatment, and even worse their results were not reproducible. In another heterogeneous system, Raney nickel was modified with amino acids and other chiral reagents to give catalysts that were used to effect asymmetric hydrogenation (9). However, it was found that the optical purities of the products were very dependent on pH and the method of catalyst preparation.

Over the past two decades, many pioneering studies directed towards catalytic asymmetric synthesis, mostly in homogeneous systems, have been undertaken. Most of the work is summarized in some review articles and books (10).

Since the first report by Wilkinson and co-workers in 1965 (11,12) concerning the catalytic activity of solutions of $[(C_6H_5)_3P]_3RhCl$ with respect to hydrogenation, extensive mechanistic studies have been carried out on this system (13). However, the detailed picture is still somewhat controversial (14,15). Wilkinson and co-workers postulated a mechanism based on kinetic data for the hydrogenation of olefins. This is outlined in Figure 1 (16). This mechanism involves the dissociated, solvent saturated species $(Ph_3P)_2RhCl(S)$ as a key intermediate.

It was envisioned that the rate-determining step could be either one or both of the two paths shown in Figure 1: (1) attack of olefin on the dihydro complex, the k' path, or "hy-

$$(PPh_3)_3RhCl \quad + \quad Solvent \ (S) \quad \rightleftharpoons \quad (PPh_3)_2RhCl(S) \quad + \quad PPh_3$$

$$(PPh_3)_2RhCl(S) \quad + \quad H_2 \quad \underset{}{\overset{K_1}{\rightleftharpoons}} \quad H_2(PPh_3)_2RhCl(S)$$

K_2 ⇅ olefin   k' ↓ olefin

$$(PPh_3)_2RhCl(olefin) \quad \xrightarrow[H_2]{k''} \quad (PPh_3)_2RhCl(S) \quad + \quad paraffin$$
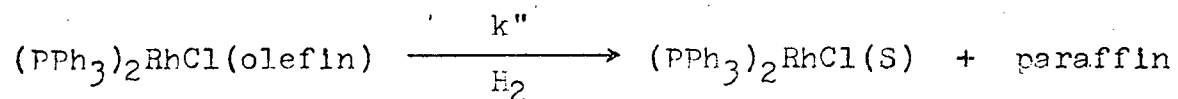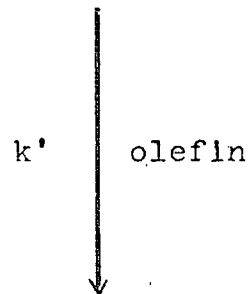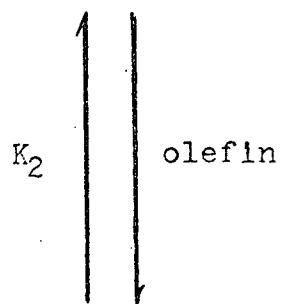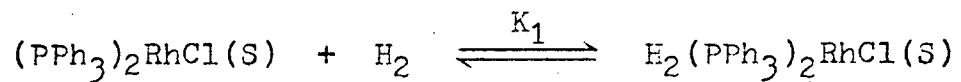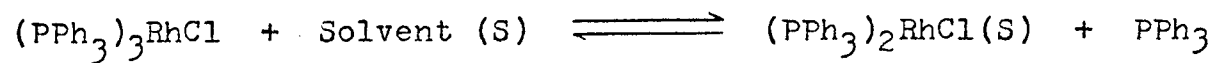
Figure 1. A proposed mechanism for hydrogenation by Wilkinson's catalyst.

dride route" (14); (ii) attack of hydrogen on the olefin
complex, the k" path, or "unsaturate route" (14). It was
found that both pathways are possible and the actual mechanism
is dependent on the choice of the substrate (14,16,17).

Contrary to the postulates of Wilkinson, Tolman et al.
found that the $RhCl(PPh_3)_3$ complex does not dissociate into
$RhCl(PPh_3)_2$ to a spectroscopically detectable extent, but is
in equilibrium with the chlorine bridged dimer $[RhCl(PPh_3)_2]_2$
(15). This dimer, which reacts with H_2 to form $H_2[RhCl(PPh_3)_2]_2$
1, was proved to be a good homogeneous hydrogenation catalyst

$$PPh_3 \quad Cl \quad PPh_3 \quad H$$
$$Rh \qquad Rh$$
$$PPh_3 \quad Cl \quad PPh_3 \quad H$$
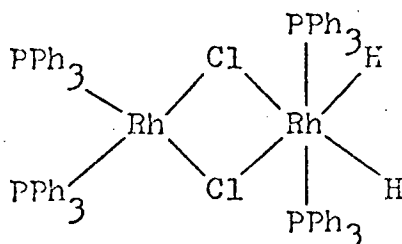
1

for the reduction of cyclohexene and ethylene. The major
paths for the hydrogenation of cyclohexene are outlined in
the following scheme:

$$\begin{array}{c} -C_6H_{12} \\ k'C_6H_{10} \end{array} \left(\begin{array}{c} [RhCl(PPh_3)_2]_2 \\ k_1 H_2 \\ H_2[RhCl(PPh_3)_2]_2 \end{array} \right) k_{-1} \rightleftharpoons \begin{array}{c} -C_6H_{12} \\ k''C_6H_{10} \end{array} \left(\begin{array}{c} 2RhCl(PPh_3)_2 \\ k_2 H_2 \\ 2H_2RhCl(PPh_3)_2 \end{array} \right) k_{-1}$$
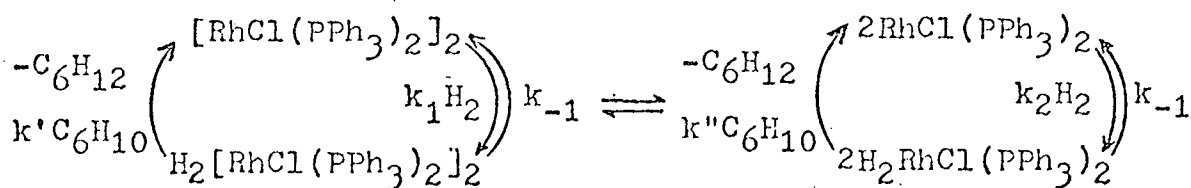
and the actual catalysts are dihydrides of bis(triphenyl-
phosphine)rhodium species.

In spite of the differences in opinion about the precise mechanism, three points on which there is a general agreement can be emphasized.

1. At some point in the catalytic cycle one phosphine ligand is dissociated, and H_2 is activated by the formation of metal-H bonds. Dimerization to $[RhCl(PPh_3)_2]_2$ also occurs after the phosphine dissociation.

2. An intermediate (or at least an activated complex) exists in which phosphine, hydrogen, and olefin are all coordinated to the metal.

3. The hydrogens are transfered successively from the central metal to the coordinated substrate which forms metal-alkyl bond first and then the leaving product.

Hydrogen activation is largely dependent on the coordination number and electronic configuration of the metal. Practically all metal complexes which are hydrogenation catalysts have a d^6 to d^8 configuration. Coordinatively saturated complexes are unreactive unless the ligands present are labile in solution. Thus it is obvious that hydrogenation catalysts are quite sensitive to solvents, substrate and ligand properties.

Halpern (18) has noted three mechanisms of activation in homogeneous hydrogenation: (i) heterolytic spliting; (ii) homolytic spliting; (iii) dihydride formation by oxidative addition. Of these, the dihydride formation appears to be the most commonly encountered. Both (i) and (iii) involve oxidative-addition of hydrogen to the metal complex. The

dihydride formation involves the addition of two hydrogen atoms, which increases the oxidation state of metal by two; whereas one hydrogen atom is added to the metal after homolytic splitting of hydrogen, which causes the oxidation number of the metal to increase by one. The general order of reactivity of metals increases from Ni to Fe, and from Fe to Os (18). Ligands such as phosphines and carbon monoxide which have both donor and acceptor properties stabilize the metal-hydrogen bond. Formation of a hydride involves either interaction of the $1s\delta$ bonding H_2 orbital with a vacant metal d orbital, or attack of an empty $1s\delta$ anti-bonding H_2 orbital upon a filled metal d or d-hybrid orbital. In the case of rhodium complexes the second alternative seems favored since $[Rh(Ph_2PCH_2CH_2PPh_2)_2]Cl$ fails to add H_2 while the more basic complexes, e.g., $[Ir(Ph_2PCH_2CH_2PPh_2)_2]Cl$ and $[Rh(Me_2PCH_2CH_2PMe_2)_2]Cl$ do (19). (The greater the basicity of the metal center the larger and more available are the d orbitals.) For a given metal ion, reactivity is enhanced by ligands which are more effective in stabilizing high oxidation states of the central metal, e.g., PPh_3, rather than CO. Thus, for example, the reactivity order toward H_2 is $Rh(PPh_3)_3Cl >$ $RhCl(CO)(PPh_3)_2$.

It has been generally accepted that coordination of the unsaturated substrate at a vacant site on the metal is necessary for homogeneous hydrogenation to proceed. This substrate activation through π-olefin coordination results in a lessening of the double bond character of the substrate and

also maintains the olefin in a favorable position for hydrogen transfer. In asymmetric hydrogenation of a prochiral substrate, the activation of the substrate seems to be a key step in producing the chiral product. (Indeed models show that the absolute configuration of the product can be predicted if the geometry of the bound olefin is taken into consideration.)

The last process in the hydrogenation reaction is the transfer of hydrogen from the metal to the π-coordinated substrate. This is generally regarded as a two step hydride transfer.

At about the same time Wilkinson reported his versatile catalyst, other groups had been working on the preparation and configurational correlation of chiral phosphines (20-24). Realizing the possibility of combining both streams of research, Horner et al. (25) hypothesized that a Wilkenson type catalyst with chiral phosphines as ligands should show asymmetric catalytic behavior.

Horner's suggestion was put into practice by Knowles and Sabacky in 1968 (26). Knowles used $P^{*}PhMePr^{\underline{n}}$ as a chiral ligand to make complexes of the type $RhL^{*}_3Cl_3$ (where L^{*} is the chiral ligand) which were used in the hydrogenation of atropic acid and itaconic acid. The reduction conditions and results are indicated in Figure 2. Although the structure of the active catalyst is not known, Knowles and Sabacky (26) suggested that the octahedral d^6 Rh(III) complexes might yield a square-planar d^8 Rh(I) complexes on reduction with H_2, which would be coordinatively unsaturated and would behave

$$Ph\text{—}\underset{\underset{\displaystyle COOH}{|}}{C}=CH_2 \quad \xrightarrow[\substack{\text{20 atm } H_2,\ 60° \\ \text{benzene-EtOH-Et}_3N}]{L^*_3RhCl_3} \quad Ph\text{—}\underset{\underset{\displaystyle COOH}{|}}{CH}\text{—}CH_3$$

atropic acid

15% e.e. (S)

$$H_2C=C\underset{\searrow COOH}{\overset{\nearrow CH_2COOH}{}} \quad \xrightarrow[\substack{\text{20 atm } H_2,\ 60 \\ \text{benzene-EtOH-Et}_3N}]{L^*_3RhCl_3} \quad CH_3\text{—}\underset{\underset{\displaystyle COOH}{|}}{CH}\text{—}CH_2COOH$$
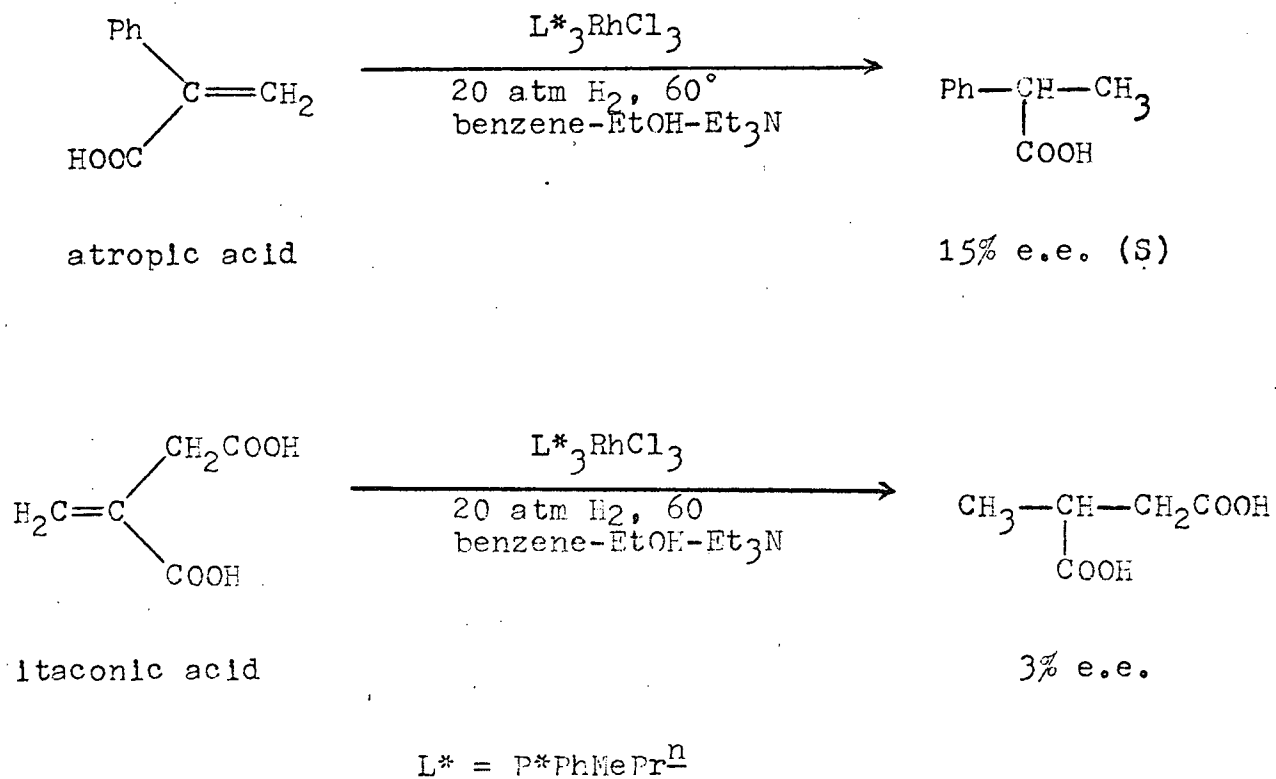
itaconic acid

3% e.e.

$$L^* = P^*PhMePr^n$$

Figure 2. Early examples of homogeneous asymmetric hydrogenation (26).

in a manner similar to Wilkinson's catalyst.

Horner et al. (27) used a catalyst prepared in situ from (S)-(+)-methylphenyl-n-propylphosphine and [Rh(1,5-hexadiene) Cl]$_2$ in benzene, a procedure designed to give neutral, square planar Rh(I) complexes of the type RhL*$_3$Cl. They envisaged the structure of the intermediate state as in Figure 3 to explain the (S)-(+)-2-phenylbutane (7-8% e.e.) obtained from α-ethylstyrene and the (R)-(+)-1-methoxy-1-phenylethane (3-4% e.e.) obtained from 1-methoxystyrene.

During studies of the hydrogenation of atropic acid with the P*MePhPr$\underline{^n}$-Rh(I) system, Knowles' group (28) found that when the L/Rh ratio was increased from 2 to 8, the hydrogenation reaction rate and optical purity increased to a maximum. This was quite peculiar since it had been established that excess ligand lowers the activity of a Wilkinson-type catalyst by competing with substrate for vacant coordination sites on the metal. It was eventually found that it was the formation of a phosphobetaine by the reaction of atropic acid with any ligand in excess of 2 equivalents per equivalent of rhodium, which influenced the rate and optical yield. Associated with this was the conversion of the substrate to the carboxylate anion (Figure 4). It was also found (28) that in the presence of triethylamine and using L/Rh = 2 a thirty-fold rate increase was observed, compared with the rate without triethylamine. An increased optical purity (28% e.e.) was also obtained.

In 1971, both Morrison's and Kagan's groups showed that in order to obtain asymmetric reduction using rhodium phosphine
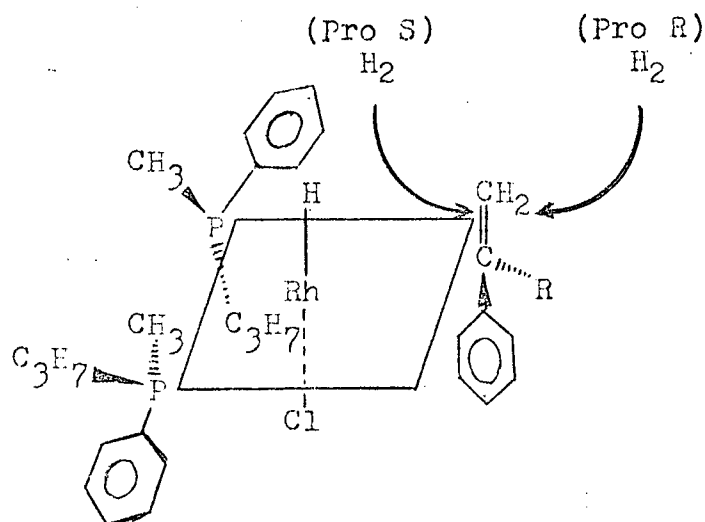
R = methyl or methoxy group.

Figure 3. A model for the correlation of the stereochemistry of reduction products with that of the chiral ligand (27).
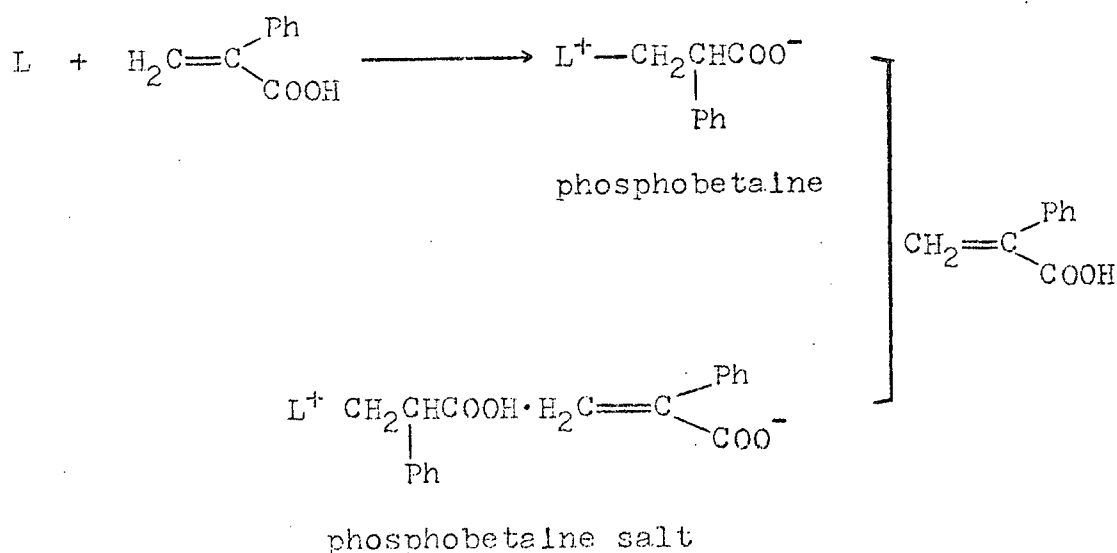
Figure 4. Reaction of a tertiary phosphine with atropic acid to produce a phosphobetaine salt.

complexes the chiral center does not have to be on phosphorus. Thus Morrison et al. (29) prepared their catalyst in situ by the reaction of (+)-neomenthyldiphenylphosphine (NMDPP) with rhodium (I) complexes of ethylene or diene in ethanol-benzene. This catalyst, thought to be Rh(NMDPP)$_3$Cl, was used to reduce (E)-β-methylcinnamic acid in the presence of trie-thylamine. The resulting 3-phenyl-butanoic acid contained a 61% e.e. of the S isomer (Figure 5). Reduction of α-ethylsty-rene gave only 7% e.e. and it was suggested that this was due to the lack of bifunctional interactions through both the carboxylate anion and olefinic bond (29,30).

Kagan and Dang used the diphosphine, (-)-2,3-0-isopro-pylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane ((-)-DIOP), 2, derived from (+)-ethyl tartarate, to prepare, in
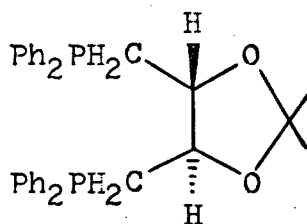
2

situ, a complex represented by [Rh(-)-DIOPClS], where S is the solvent (31,32). This solution catalyzed the reduction of alkenes at room temperature and atmospheric pressure. Thus α-acetamidocinnamic acid was reduced to (R)-N-acetyl-phenylalanine with an optical yield of 72%, the chemical yield being 95%. They attributed the high stereoselectivity

(E)-β-methylcinnamic acid

61% e.e. (S)

$[Rh(CH_2=CH_2)_2Cl]_2$, NMDPP

20 atm H_2, 60°
benzene-EtOH-Et_3N

NMDPP = H$_3$C····⟨⟩—Pr^i ≡

PPh$_2$
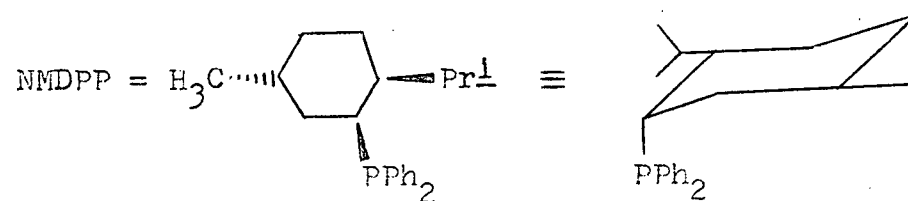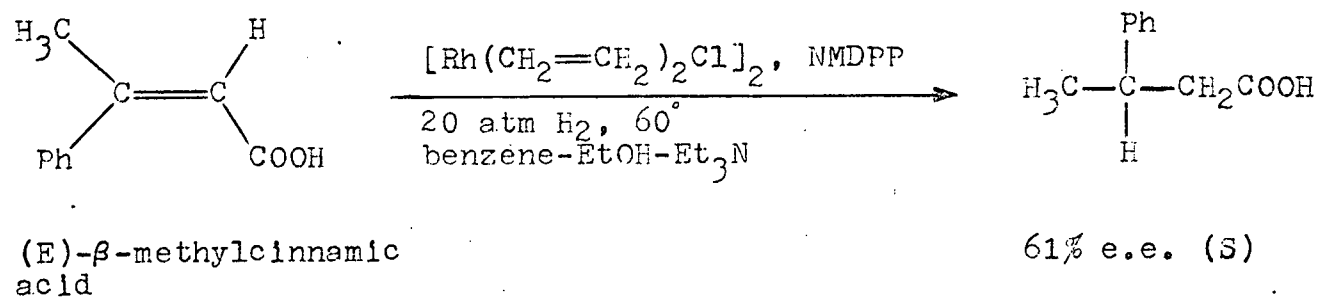
Figure 5. Asymmetric homogeneous hydrogenation with a neomenthyldiphenyl-
phosphine (NMDPP) catalyst (29).

of this reduction to the conformational rigidity of the trans-
fused dioxolane ring and also to the presence of the rhodium-
containing chelate ring. Stereochemical control through par-
ticipation of the carboxylic acid function of the substrate
also seemed to be indicated since hydrogenation of methyl α-
phenylacrylate gave methyl-2-phenylpropanoate of the R confi-
guration in only 7% e.e. (31). Later, it was found that a
substrate containing the enamide group could be hydrogenated
with high optical yield (32). For example, $CH_3CH=C<^{NHCOCH_3}_{Ph}$
was hydrogenated to afford a 78% optical yield. Table 1 shows
the results obtained by Kagan et al. with DIOP as the ligand
in the hydrogenation of α-acylamidoacrylic acids. They found
that the Rh-(-)-DIOP catalyst gave the unnatural R or D-amino
acid derivatives, whereas L-amino acid derivatives could be
obtained with the (+)-DIOP catalyst.

In 1972, Knowles and co-workers (30,33-36) synthesized
chiral o-anisylcyclohexylmethylphosphine (ACMP) 3. This
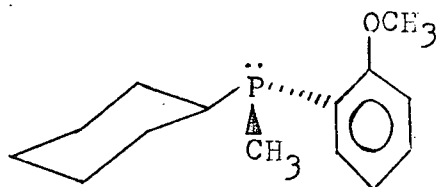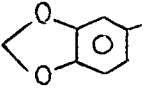
3 (+)-(R)-ACMP

ligand gave complexes with rhodium, which were very effective
catalysts for the reduction of α-acylamidoacrylic acids. Op-
tical yield as high as 90% were obtained. Catalysts prepared

Table 1. Asymmetric Hydrogenations of α-Acylamidoacrylic
Acids with the Soluble DIOP Catalyst (32).

$$R'HC{=\!=}C\begin{smallmatrix}NHCOR\\[4pt]COOH\end{smallmatrix} \longrightarrow R'CH_2\underset{\underset{COOH}{|}}{C}HNHCOR$$

R'	R	Conversion (%)	Optical yield (%)
H	CH$_3$	96	73
Ph	CH$_3$	95	72
p-OH-phenyl	CH$_3$	92	80
	CH$_3$	97	79
p-OH-phenyl	Ph	95	62
i-C$_3$H$_7$	Ph	98	22

[a][Rh] = 3 mM; P = 1.1 atm; room temperature. [b](-)-DIOP-Rh
complex gives D amino acid derivatives; (+)-DIOP-Rh complex
gives L.

from (+)-ACMP give L-amino acid derivatives and (-)-ACMP give D-amino acid derivatives. In 1975, they obtained an enantiomeric excess of 96% in the reduction of α-acylamidoacrylic acids using a new chiral di(tertiary phosphine) 4 as the li-

$$
\begin{array}{c}
C_6H_5 \\
| \\
(: P \text{''''} CH_2)_2 \\
\uparrow \\
OCH_3
\end{array}
$$

4
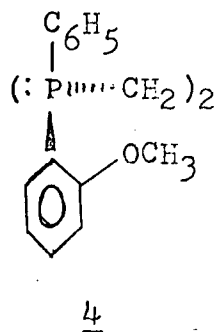
gand (37). The catalytic species was believed to be in the cationic form. They found that the high optical yields obtained with this chelating ligand were not sensitive to temperature and pressure change.

While different kinds of "Wilkinson type" catalysts were being developed, Osborn and his co-workers were working on cationic rhodium systems. These proved to be useful as hydrogenation and hydrosilylation catalysts (37,39-44). They have the formula $[(diene)Rh\ L_n]^+$ and are efficient at 25° and 1 atm of H_2. They are easy to make in large numbers since L can vary widely and can be isolated for physical studies. These cationic catalytic systems are very versatile, for example, some will reduce alkynes specifically to cis olefins (43), chelating dienes to monoenes (43), and ketones to alcohols (39,41,44). Knowles used his asymmetric ligands, ACMP

3 and di(tertiary phosphine) 4, to make cationic rhodium com-
plexes which catalyzed the reduction of α-acylamidoacrylic
acids giving optical yields as high as 96% (33,37). In later
studies, however, Knowles found that the in situ preparation
of rhodium (I) catalysts gave the same results as using the
crystalline, air stable, cationic complexes [Rh(1,5-cyclo-
octadiene)(ACMP)]⁺BF₄⁻ or BPh₄⁻ (33). In these latter experi-
ments the catalyst was prepared by adding the phosphine ligands
to alcoholic solutions of [Rh(diene)Cl]₂. Two ligands per
rhodium were shown to give optimum results, just as expected
for the formation of cationic complex species.

In 1976, Kagan prepared a cationic rhodium complex with
(+)-DIOP as the ligand. An optical yield of 92% was attained
in the asymmetric reduction of N-acetyl-1-phenyl-1-aminopropene
(46). A tentative hydrogenation intermediate 5 was proposed
as follows but with little substantiation:

5
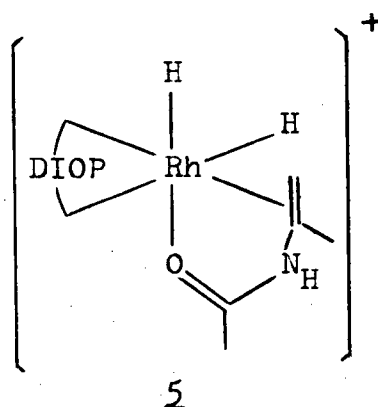
Complexes of Co and Ru have also been used for the asym-
metric hydrogenation of prochiral olefins (47,48); but most
results are not very satisfactory. However, recently an op-

tical yield of 60% for the hydrogenation of α-acetamidoacrylic acid has been obtained using $[Ru_2Cl_4(DIOP)_3]$ as the catalyst (49).

Present Studies

Since the discovery of ferrocene in 1951 (50,51), there have been many investigations of the chemistry of this sandwich compound, especially relating to it stereochemistry (52-56). This interest was due in part to the recognition that ferrocene derivatives are chiral if one ring carries two different substituents X and Y. 6 and 7 are two cases in

6   7
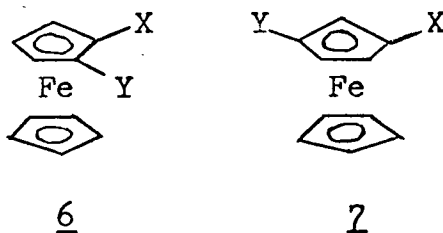
which this may happen and should be noticed that these compounds are optically active even though there is no center of asymmetry but only a planar element of chirality. A study by Ugi and co-workers (57) found that ferrocene derivatives with a plane of chirality exhibit a strong asymmetric inducing power, without having large steric bulk close to the reactive site. This is in contrast with the asymmetrically inducing steric templates that contain only central elements of chirality, where one extremely bulky group, a medium sized group, a small group and the reactive site usually constitute the

four ligands of the inducing central chiroid (58-62).

At the begining of the present study, it was decided to attempt the synthesis of (+)- and (-)-(2-diphenylphosphino-ferrocenyl)ethyldimethylamines ((+)- and (-)-FcNP) and use them as asymmetric ligands in rhodium complexes. It was expected that (+)- and (-)-FcNP would be easy to prepare because it had been shown that lithiation of (R)-N,N-dimethyl-1-ferrocenylethylamine ((R)-FcN) with butyllithium in ether-hexane affords only the ortho lithiation products (55,63), which consists of a 96:4 mixture of (R,R)- and (R,S)-FcNLi as measured by gas chromatography following treatment with trimethylchlorosilane (55). Thus treatment of the lithiated products with chlorodiphenylphosphine would be expected to yield (R,S)-FcNP (96%) and (R,R)-FcNP (4%). The overall reaction is shown in the following scheme:

(R,R)-FcNLi   (R,S)-FcNP

(R)-FcN

(R,S)-FcNLi   (R,R)-FcNP
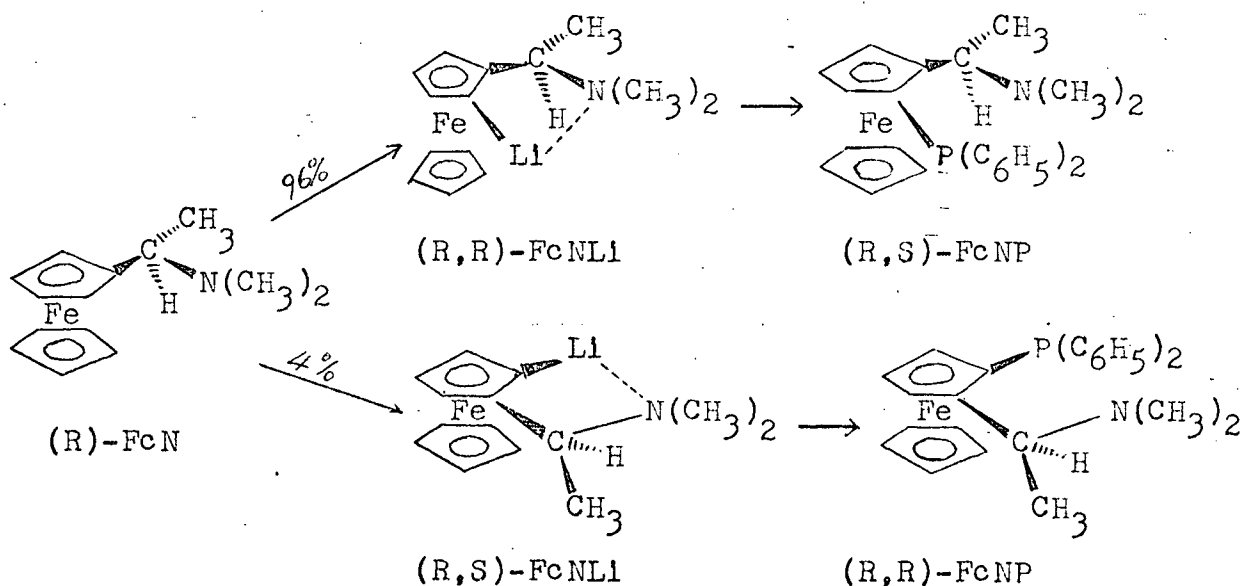
The same scheme applied to the (S)-isomer of N,N-dimethyl-1-ferrocenylethylamine should afford 96% of (S,R)-FcNP and 4% (S,S)-FcNP. It is very interesting to note from Figure 6 that (R,S)-FcNP and (S,R)-FcNP, instead of being diastereomers of each other, are enantiomers.

A preliminary communication has described ligand (S,R)-FcNP and its use in a rhodium complex to catalyze the hydrosilylation of ketones (64). It is of interest to study the hydrogenation of prochiral substrate with both (S,R)- and (R,S)-FcNP as the catalyst ligand and one aim of the present work was to prepare and isolate the catalyst or catalyst precursor, in order to determine its solid state structure. This would be of value in visualizing the reaction intermediate which in turn would help in rationalizing the configuration of the reduction products.
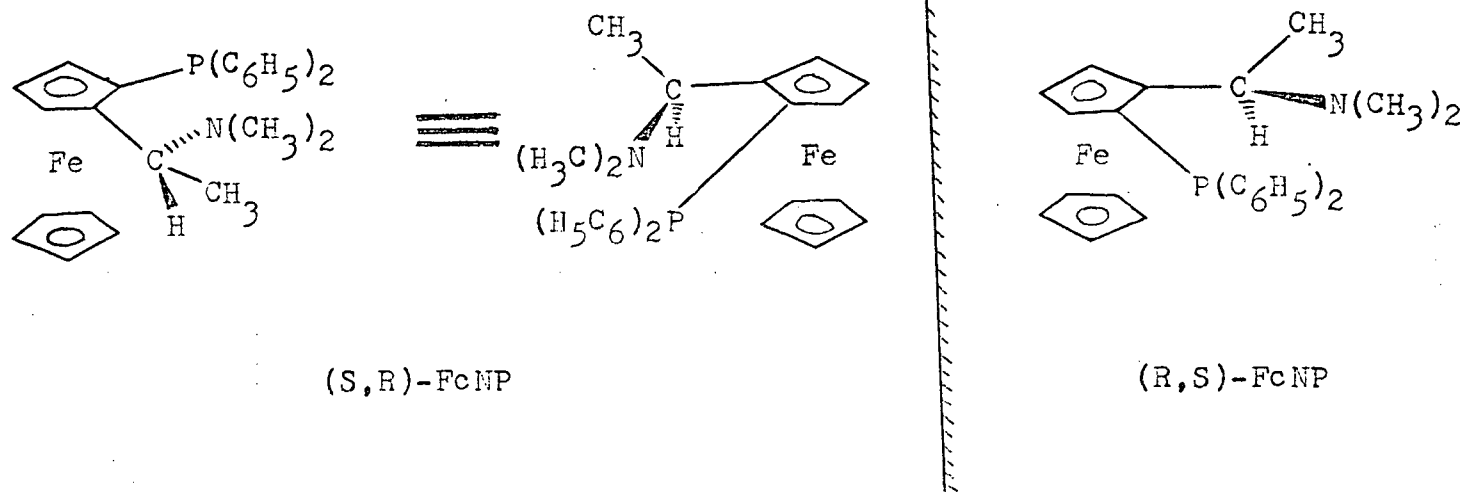
Figure 6. The enantiomeric relationship of (R,S)- and (S,R)-FcNP.

EXPERIMENTAL

General

Unless otherwise specified all chemicals were purchased from commercial sources and were used as received.

In particular, dry diethyl ether was obtained from Mallinckrodt and was used without further drying. Tetrahydrofuran (THF) was distilled from LiAlH$_4$ and was stored under nitrogen over molecular sieves. Benzene was refluxed over potassium wire and stored under nitrogen over molecular sieves. Ethanol was distilled from LiAlH$_4$ and was stored under nitrogen over molecular sieves. Spectro grade methanol from MCB and reagent grade isobutanol from AMACHEM were used without purification but were vacuum degassed before use.

Hydrogen was obtained from Canadian Liquid Air and was passed through a "Deoxo" catalytic purifer before use.

Conductivity measurements were made in nitromethane at 25° with Wayne Kerr Universal Bridge B221A.

Infrared spectra were measured on a Perkin-Elmer 457 spectrometer. Carbonyl frequencies were measured on a Unicon SP1100 Infrared Spectrophotometer. Spectra were calibrated using a polystyrene film.

NMR measurements were made on either Varian Model HA-100 or T-60 instruments operating at room temperature. Chemical shifts are given in ppm downfield from internal TMS.

Optical rotations were measured on a Perkin-Elmer 141 polarimeter. The sodium-D line of wave length 589 nm was used

as the monochromatic light source.   An optical cell of 1 cm
path length was used.

Melting points were determined using a Gallenkamp Melting
Point apparatus and are reported without correction.

All microanalyses were done by Mr. Peter Borda of this
department.

Hydrogenation Apparatus

The apparatus used for hydrogenation is shown schema-
tically in Figure 7.   The reaction flask A consists of two
compartments A1 and A2, which are used to accommodate substrate
and catalyst respectively.   The U-shaped oil manometer was
filled with butyl phthalate which has negligible vapor
pressure.   A measuring burette I of volume 50 ml and length
about 90 cm was mounted on the line at one end and at the
other end was connected to the mercury reservior C.   The
reaction flask was thermostated in a paraffin oil bath in-
sulated with polystyrene foam.   Constant temperature was
maintained by JUMO-MSD.B.P. thermoregulator and JUMOGKT10-0
relay control unit.   Heating was supplied by a 25 watt elon-
gated light bulb.   A 3' magnetic stirrer was used in the
thermostat bath and a 0.5' magnetic stirrer was used in the
reaction flask A.

Experimental procedure for a typical gas uptake experiment

The catalyst precursor and the substrate were measured
out to $\pm$0.1 mg and placed in A2 and A1 respectively.   The

E CAP 1

CAP 2

A

A2   A1

F

B

I

C

H

TO
VACUUM

G

GAS INLET
(N_2 AND H_2)
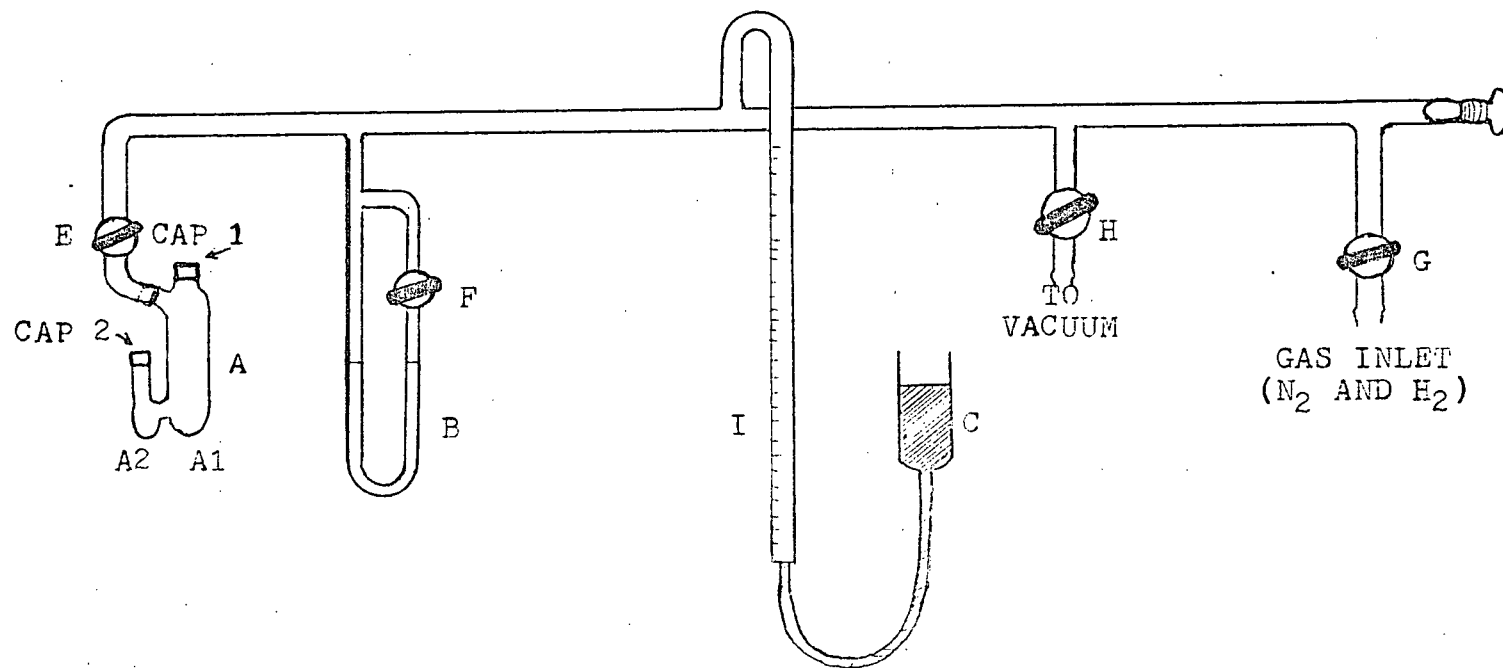
Figure 7.   A schematic drawing of the catalytic hydrogenation apparatus.

flask A was evacuated and filled with N_2. Cap 1 was opened
and 10 ml of solvent was added while flushing with nitrogen.
Cap 1 was closed and the solution (substrate and solvent) was
degassed by pumping for a few seconds. E was closed and the
reaction line was evacuated through H while F was open and G
closed. A was frozen with liquid nitrogen and E opened to
remove all air from the reaction flask. E was closed, the
nitrogen coolant was removed and nitrogen gas was admitted to
the rest of the line up to tap E. The gas inlet G was closed
and E was open to let nitrogen into A. E was closed and the
frozen solvent was thawed. Flask A was tilted to wash the
catalyst precursor into A and the mixture was stirred to
obtain complete solution. The solution (substrate, solvent
and catalyst) was frozen again. A was evacuated and then
thawed again after closing E. The flask was thermostrated
to the required temperature and hydrogen was admitted into
the line up to E. The gas inlet G was closed and E was opened
to admit H_2 to the whole system at a pressure less than 1 atm.
After thermal equilibrium had been reached (this was checked
by closing F and observing any change in the oil levels of
the manometer.) G was opened to admit more hydrogen until
the mercury levels of I and C were the same and F was closed.

Any gas uptake was accompanied by a rise in the level of
the oil manometer. The pressure loss was compensated by
raising the mercury reservoir until the two oil column were
leveled again. The mercury level of the measuring burette
was monitored as a function of time. No attempt was made to

correct the data for any contribution from the solvent vapor to the pressure.

Isolation of hydrogenation products

N-Acetylphenylalanine The product, after pumping off the solvent, was washed with 4 ml of dichloromethane three times. N-acetylphenylalanine is insoluble in CH_2Cl_2 and in this way the product was separated from catalyst without altering its form. (Recrystallization from water could result in enrichment of one enantiomer and an artificially high optical yield.)

N-Acetylalanine The mixture was dissolved in 10 ml of water after the solvent had been removed by pumping. It was then filtered through celite twice. The product was obtained after freeze drying the aqueous solution.

Preparation of Acetylferrocene (65)

Ferrocene (93 g, 0.5 mole) was dissolved in 400 ml of dry dichloromethane in a 1 l flask equipped with a 2 in. magnetic stirring bar and fitted with a drying tube ($CaCl_2$). Acetyl chloride (43 g, 0.55 mole) was added. The flask was then immersed in an ice water bath of 0-5°. Anhydrous aluminum chloride (67 g, 0.5 mole) was added in about 10 portions with 2-5 min. between each portion to allow heat exchange. The reaction was vigorous and the color of the solution changed from red-brown to deep wine-red. The reaction mixture

was stirred for 2 hours as the ice water bath gradually warmed to room temperature. The reaction mixture was hydrolyzed by the slow addition of 100 ml cold water in 5 ml portions while the whole flask was immersed in cold water bath. An additional 120 ml of water was then added more rapidly. The cold water bath was removed and about 50 ml of freshly prepared 10% aqueous $Na_2S_2O_4$ solution was added dropwise with stirring until the upper layer changed color from brown to cream-yellow. The solution was stirred for about one hour until the odor of SO_2 was undetectable.

The reaction mixture was separated and the aqueous layer extracted three times with 100 ml portion of dichloromethane. The organic extracts were combined and washed with 100 ml of 5% aqueous NaOH solution and 100 ml of saturated aqueous NaCl solution. The solution was dried over anhydrous K_2CO_3 overnight, filtered, and the solvent was evaported to give 110 g (95%) of the orange solid product, mp 87°. (lit. mp 85-86° (65))

Preparation of α-Ferrocenylethanol (65)

Acetylferrocene (25 g, 0.11 mole) was dissolved in anhydrous ether (500 ml) in a 4-necked 1 l flask equipped with a reflux condenser, nitrogen inlet, magnetic stirrer and dropping funnel. The solution was stirred and slowly treated dropwise with a suspension of 2.2 g of $LiAlH_4$ in ether and then heated under reflux for two hours. The excess of $LiAlH_4$ was destroyed by the slow addition (4°) of ethyl acetate and

the resulting reaction mixture was treated with a saturated solution containing 30 g of NH$_4$Cl in water. After being stirred 0.5 hour at 0°, the reaction mixture was filtered and the organic layer separated. The ether solution was washed twice with water and then concentrated to dryness to yield 22.5 g of a yellow solid, mp 74°. This product was pure enough to use directly but a portion of it was recrystallized from n-heptane to give yellow needles, mp 79° (lit. mp 78-79° (65)).

Preparation of α-Ferrocenylethyl Acetate (65)

α-Ferrocenylethanol (69 g, 0.3 mole) and acetic acid (20 ml, 0.33 mole) were dissolved in 500 ml of reagent grade benzene and placed in a 1 l round bottom flask fitted with a water separator (Dean and Stark trap), and a reflux condenser with a drying tube on top. Some boiling chips were added and the solution was refluxed overnight.

The reaction mixture was cooled, decanted from the boiling chips, and evaporated to afford about 80 g of a dark red-brown oil. The product was not purified and was used directly.

Preparation of N,N-Dimethyl-α-Ferrocenylethylamine (65)

α-Ferrocenylethyl acetate (68 g, 0.25 mole) was dissolved in about 1400 ml of methanol in a 2 l conical flask to which was added 240 ml of 25% aqueous dimethylamine. The mixture was stirred for three days at room temperature.

The solvent was evaporated leaving a dark oily residue which still contained some water. This was stirred with a mixture of 300 ml 8.5% aqueous phosphoric acid and 100 ml of ether. The layers were separated and the acid aqueous solution was washed with 100 ml of ether to remove neutral by-products. The dark green acidic solution of the amine was neutralized by cautious addition of Na_2CO_3, allowing the effervescence to subside before each subsequent addition. The process was continued until no more effervescence was observed and by that time the dark green solution had turned yellow-brown. The amine was extracted with three 100 ml portions of dichloromethane and washed with 100 ml of water, dried over K_2CO_3 ($MgSO_4$ cannot be used) and evaporated to give about 50 g of a dark red-brown oil which was rapidly vacuum distilled to avoid decomposition. bp. 118°/0.5 mmHg (lit. 120°/2 mmHg (65)). The yield was about 45 g.

Resolution of N,N-Dimethyl-α-Ferrocenylamine (65)

The racemic amine (25.7 g, 0.1 mole) and 15 g of R-(+)-tartaric acid were each dissolved in 50 ml of methanol in 250 ml flasks. Both flasks were immersed in a hot water bath at about 55° for about 10 min. to reach thermal equilibrium. The tartaric acid solution was then poured into the amine solution while stirring. The temperature of the bath was allowed to fall at a rate of 2-5°/hour. Occasional scratching the flask with a glass rod was required to aid solid formation. Stirring was continued overnight and

about 15 g of the (-)-amine tartarate was collected. The
mother liquor was set aside for later use. The tartarate
salt was added to about 50 ml of 20% aqueous NaOH solution
in a separatory funnel and the amine extracted with three
25 ml portions of dichloromethane. The amine solution was
dried over K_2CO_3 and evaporated to give the optically active
amine as dark oil.

The amine thus obtained and 5.55 g of tartaric acid,
each in 25 ml of methanol were mixed and seeded as above to
afford the amine tartarate salt. This affords 9 g of opti-
cally active (-)-amine, $[\alpha]_D^{25}$ -12° (c 1, 95% ethanol), (lit.
$[\alpha]_D^{25}$ -14° (c 1, 95% ethanol) (65)) when treated with base as
above.

The mother liquor from the first crystallization was
concentrated to about one-fourth of its original volume.
Diethyl ether was added slowly to the solution until preci-
pitation was complete. The mixture was left at 0° overnight
and 24.3 g of (+)-amine tartarate was collected. The (+)-
amine tartarate crystals were recrystallized by dissolving
them in about 30 ml of hot water followed by the addition of
about 300 ml acetone. Fine needle crystals of the (+)-amine
tartarate were obtained in this modified way. Optically
pure (+)-amine, $[\alpha]_D^{25}$ 14.5° (c 1, 95% ethanol) (lit. $[\alpha]_D^{25}$
14° (65)) was obtained from the tartarate as described above
for the (-)-isomer.

Preparation of (S,R)- and (R,S)-FcNP (66,67)

At 23°, 10 g of (R)-(+)-FcN was dissolved in 60 ml anhydrous diethyl ether in a two-necked 250 ml round bottom flask equipped with a magnetic stirrer and a reflux condenser. To this solution was added dropwise 21 ml of 2.2 M n-butyllithium in n-hexane. The reaction was slightly exothermic and the color of the mixture changed from red-brown to orange red. After stirring 1.5 hours, the mixture was slowly treated with 17.5 g of chlorodiphenylphosphine. This reaction was very exothermic and the color turned to yellow with the precipitation of LiCl. The mixture was refluxed for 2 hours and then cooled to room temperature. An aqueous slurry of $NaHCO_3$ (80 ml) was added to the reaction mixture very slowly while stirring. The mixture was stirred for about 20 min. to hydrolyze the product. The solid was filtered off and washed with diethyl ether until all the orange yellow compound had been dissolved. The ether layer was separated, added to the washings and dried over $MgSO_4$. After evaporating to dryness, the dark brown oil was cooled to 4° overnight to afford a brown yellow solid which was recrystallized from ethanol to yield 6 g of brown yellow crystals of (R,S)-(-)-FcNP, mp 136°, $[\alpha]_D^{25}$ -364° (c 0.42, ethanol). (S)-(-)-FcN was treated in the same manner to yield (S,R)-(+)-FcNP, mp 135°, $[\alpha]_D^{25}$ +361.4° (c 0.381, ethanol), (lit. mp 139°, $[\alpha]_D^{25}$ +361° (c 0.6, EtOH), (64)). Anal. Calc. For $C_{26}H_{28}FcNP$: C, 70.7; H, 6.35; N, 3.17. Found: C, 70.4; H, 6.33; N, 3.14%. ^{1}H NMR ($CDCl_3$) 1.17 (d,

J=7 Hz, C-CH$_3$), 1.80 (s, N(CH$_3$)$_2$), 3.9 (s, FeC$_5$H$_5$), 3.5-4.5 (m, FeC$_5$H$_4$ mixed with C-H), 6.9-7.85(m, C$_6$H$_5$). The NMR and analytic data were obtained from the racemic mixture.

Preparation of [(NBD)RhCl]$_2$ (68)

Rhodium trichloride trihydrate (0.7 g) was dissolved in 95% ethanol (10 ml) in a 100 ml Schlenk tube and 2 ml of nor-bornadiene (C$_7$H$_8$) was added to the solution. The tube was flushed with nitrogen and sealed with a serum cap. A yellow precipitate appeared about 15 minutes after the reactants had been mixed. The reaction mixture was stirred for two days. The yellow deposit was isolated and recrystallized from chloroform-petroleum ether to give fine yellow crystals.

Preparation of [(COD)RhCl]$_2$ (69)

In a 100 ml three-necked round bottom flask was dissolved rhodium trichloride trihydrate (1 g) and 1,5-cyclooctadiene (2 ml) in 30 ml of 95% ethanol. The solution was heated and refluxed for 3 hours. The orange yellow crystalline product was filtered and washed with ethanol and then recrystallized from acetic acid to afford orange yellow crystals.

Preparation of [(C$_8$H$_{14}$)RhCl]$_2$ (70)

Rhodium trichloride trihydrate (1 g) was dissolved in 99.5% ethanol (20 ml) in a 100 ml Schlenk tube. Cyclooctene (3 g) was added to the solution and the mixture was sealed

under nitrogen, and was kept at room temperature for three days. A red brown solid was formed (0.85 g). The product was isolated and washed with a small quantity of absolute ethanol, then dried and stored under nitrogen in the refrigerator (T<5°).

Preparation of [Rh(CO)₂Cl]₂ (71)
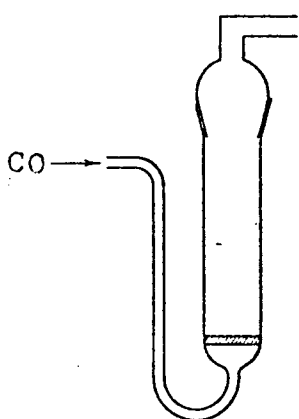
An apparatus, shown as Figure 8, with a porous disk (medium porosity) was set up in the fume hood. Rhodium trichloride trihydrate (1 g) was pulverized and placed on the top of the disk. The apparatus was flushed slowly with CO and immersed in an oil bath maintained at 96-100°. The water vapor which condensed at the top of the tube was removed occasionally with absorbent cotton. Orange red crystals of product sublimed to about half way up the tube. When the reaction was completed, (about 4 hours) the apparatus was removed from the oil bath and cooled. The crystals were scraped from the reaction vessel to give about 0.75 g of pure product, mp 124-126° (lit. 124-125° (71)). The crystals were stored in a refrigerator (T<-5°).

Figure 8.

Preparation of (Acac)Rh(COD) (72)

A mixture of [(COD)RhCl]₂ (0.761 g), diethyl ether (17 ml)

and acetylacetone (0.61 ml) in a 200 ml Schlenk tube with a
magnetic stirring bar was chilled to -78° and a solution of
1 g of KOH in 3.3 ml of water added dropwisely. The mixture
was warmed to 0° with stirring, and later, a further 17 ml of
diethyl ether was added. This mixture was stirred at 0° for
0.5 hour. The ether was separated, filtered and chilled to
-78° again. The yellow crystals which precipitated were
separated and dried. The filtrate was concentrated and
chilled again and more crystals were deposited, mp 125°. Anal.
Calc. for $C_{13}H_{19}O_2Rh$: C, 50.3; H, 6.13; Found: C, 50.4; H,
6.40%.

Preparation of [(FcNP)Rh(CO)Cl] (91)

[Rh(CO)$_2$Cl]$_2$ (0.13 g) was dissolved in 2.5 ml of benzene
in a 100 ml Schlenk tube. On addition of 25 ml of benzene
containing 0.3 g of FcNP, CO was evolved and the colour
changed from orange yellow to red. The solution was evaporated
under vacuum to dryness and a yellow brown solid remained.
The solid was dissolved in a minimum quantity of degassed
CH_2Cl_2 and diethyl ether was slowly added until slight turbu-
lence was seen. The mixture was cooled to 5° and solid formed
in about one hour. The solvent was removed and the solid
product was washed with ether, and recrystallized from ben-
zene, mp 124-125°. ν(CO), 1990 cm^{-1} (cyclohexane). Anal.
Calc. for $C_{33}H_{34}ClFeNOPRh$: C, 58.2; H, 4.99; N, 2.05; Cl, 5.21.
Found: C, 58.1; H, 5.10; N, 1.80; Cl, 5.08%. ^{1}H NMR (CDCl$_3$)

1.25 (d, J=7 Hz, C-CH$_3$), 2.47 (s, N-CH$_3$), 3.14 (s, N-CH$_3$), 3.79 (s, FeC$_5$H$_5$), 3.9-4.7 (m, FeC$_5$H$_3$ mixed with C-H), 6.9-7.9 (m, C$_6$H$_5$).

Preparation of (FcNP)Ni(CO)$_3$ (73)

FcNP (3.4 g, 7.7 mmole) was dissolved in 33 ml of diethyl ether in a 3-necked, 100 ml flask equipped with a reflux condenser, nitrogen inlet, and magnetic stirrer. The solution was heated in an efficient fume hood to the reflux temperature and Ni(CO)$_4$ (1.31 g, 7.7 mmole) was added to the solution. The reaction mixture was refluxed for 30 minutes, then it was cooled to room temperature. An orange yellow solid was formed which was washed with diethyl ether to afford 3.1 g of orange yellow crystals, mp 135°. Anal. Calc. For C$_{29}$H$_{28}$FeNNiO$_3$P: C, 59.6; H, 4.79; N, 2.40. Found: C, 59.4; H, 4.83; N, 2.44%. ν(CO), 1980, 2000, 2060 cm^{-1} (cyclohexane).

Preparation of [(NBD)Rh(FcNP)]$^+$PF$_6^-$ (74)

[(NBD)RhCl]$_2$ (250 mg, 0.56 mmole) dissolved in 8 ml C$_6$H$_6$ and FcNP (0.685 g, 1.55 mmole) dissolved in 2 ml THF were combined together in a 100 ml Schlenk tube, and to this mixture was added NH$_4$PF$_6$ (0.171 g) in acetone. The fine precipitate, which formed immediately, was filtered and washed with dichloromethane. After concentrating the filtrate and washings under reduced pressure, two phases formed. The turbid bottom phase was isolated and further concentrated to about half its

volume. Red solids separated at this time and more came out after standing 12 hours at room temperature. If no solid precipitated, ethanol was added very slowly until a slight turbulence was seen then a drop of diethyl ether was added. The mixture was cooled to 4° overnight to afford a red solid which was washed with diethyl ether and dried. The solid was recrystallized from a minimum quantity of dichloromethane by the addition of ethanol and diethyl ether and red fine crystals resulted, mp 192° (decomp.). Anal. Calc. for $C_{33}H_{36}FeF_6NP_2Rh$: C, 50.7; H, 4.61; N, 1.79. Found: C, 47.7; H, 4.78; N, 1.48%. $\Lambda = 72.3$ ohm^{-1}cm^{-1}M^{-1}. ^{1}H NMR (CDCl$_3$) 1.78 (d, J=6.4 Hz, C-CH$_3$), 2.42 (s, N-CH$_3$), 3.19 (s, N-CH$_3$), 3.61 (s, FeC$_5$H$_5$), 1.46 (s, methylene), 4.16 (s, methine), 4.44 (m, FeC$_5$H$_3$), 7-8.5 (m, C$_6$H$_5$)

Preparation of [(COD)Rh(FcNP)]$^+$ClO$_4^-$ (74)

Rh(COD)(acac) (250 mg, 0.81 mmole) was placed in a Schlenk tube into which 3 ml of THF and 115 mg (approximately 1 drop) of 70% HClO$_4$ in 1 ml of THF was added under an Ar atmosphere. Addition of FcNP (800 mg, 1.81 mmole) changed the color of the solution from yellow to orange-red. The solvent was removed and the resultant solid dissolved in a minimum quantity of boiling 95% ethanol, cooled to room temperature, and stored at 4° for four hours. A dark solid formed. The solid was isolated and washed with ether. The solid was recrystallized from ethanol to yield orange-red crystals, mp 185° (decomp.). Anal. Calcd. for $C_{34}H_{40}ClFeNO_4PRh$: C, 55.2; H, 5.41; N, 1.89.

Found: C, 54.6; H, 5.09; N, 1.90%. $\Lambda = 73.6$ ohm^{-1}cm^{-1}M^{-1}.

Preparation of [(COD)Rh(FcNP)]$^+$BF$_4^-$ (74,75)

To a Schlenk tube purged with N$_2$ was added [(COD)RhCl]$_2$ (0.246 g, 5 mmole) followed by 3 ml of methanol with stirring. FcNP (0.53 g, 1.2 mmole) dissolved in about 10 ml of methanol was added to the mixture. After stirring for 20 min. the slurry had become an orange-red solution. NH$_4$BF$_4$ (0.14 g) in 1.6 ml of H$_2$O was added while stirring, and an orange-red solid precipitated. This was separated, washed with 1 ml of H$_2$O and 1 ml of methanol, and recrystallized from ethanol. These fine orange-red crystals were washed with diethyl ether and dried under reduced pressure, mp 190° (decomp.). Recrystallization could also be achieved by dissolving the solid in a minimum quantity of CH$_2$Cl$_2$ and adding ethanol. Anal. Calcd. for C$_{34}$H$_{40}$BF$_4$FeNPRh: C, 55.2; H, 5.41; N, 1.89. Found: C, 55.2; H, 5.31; N, 1.89%. $\Lambda = 73.9$ ohm^{-1}cm^{-1}M^{-1}. ^{1}H NMR (CDCl$_3$) 1.01-1.61 (m, methylene), 1.87 (d, J=6.2 Hz, C-CH$_3$), 2.71 (s, N-CH$_3$), 3.30 (s, N-CH3), 3.56 (s, FeC$_5$H$_5$), 4.16-4.46 (m, FeC$_5$H$_3$ mixed with C-H), 5.06 (s, olefin), 5.61 (s, olefin), 7.06-7.76 (m, C$_6$H$_5$).

Preparation of [(NBD)Rh(FcNP)]$^+$ClO$_4^-$ (74)

[(NBD)RhCl]$_2$ (130 mg, 0.28 mmole) was dissolved in 4 ml of benzene in a Schlenk tube to which was added FcNP (0.3564 g, 0.81 mmole), and a solution of NaClO$_4$ (86.9 mg) in 1.3 ml

of THF. The suspension was further stirred for 5 min. before 2 ml of diethyl ether was added to complete the precipitation. The solid was separated, washed with 2.5 ml of benzene and 2.5 ml of diethyl ether, and dried. The yellow solid was dissolved in 1 ml of dichloromathane and filtered to remove solid impurities. After adding ethanol and diethyl ether to the filtrate a yellow solid formed which turned into orange brown crystals after storing at 0° for 12 hours, mp 190° (decomp.) Anal. Calcd. for $C_{33}H_{36}ClFeNO_4PRh$: C, 53.8; H, 4.89; N, 1.90. Found: C, 53.5; H, 4.84; N, 1.83%.

Preparation of $[(COD)Rh((-)-FcNP)]^+B(C_6H_5)_4^-$ (74)

$[(COD)RhCl]_2$ (0.1255 g, 0.25 mmole) was dissolved in methanol in a Schlenk tube under argon. To this was added FcNP (0.4484 g, 1.06 mmole) and the mixture was stirred. More methanol was added to dissolve any remaining solid. Solid sodium tetraphenylborate (0.1095 g) was added and stirring was continued for 10 min. The orange yellow solid which precipitated was filtered and washed with benzene and diethyl ether and dried under reduced pressure, mp 150-152° (decomp.). Anal. Calcd. for $C_{58}H_{60}BFeNPRh$: C, 71.7; H, 6.22; N, 1.44. Found: C, 71.4; H, 6.10; N, 1.44%. $\Lambda=50.13$ $ohm^{-1}cm^{-1}M^{-1}$.

RESULTS AND DISCUSSION

Synthesis of The Chiral Phosphine Ligands (+)-, (-)-FcNP

As mentioned in the Introduction, it was decided to
attempt the synthesis of chiral ferrocenylphosphine ligands
((R,S)- and (S,R)-α-[2-diphenylphosphinoferrocenyl]ethyldi-
methylamine or (R,S)- and (S,R)-FcNP) which not only have an
asymmetric center at carbon but also have planar chirality.
In addition, this ligand would contain a heavy ferrocene
group which might show some steric and electronic effects in
asymmetric hydrogenation reactions.

The precursors of the ligands ((R)- and (S)-FcN) and
related compounds have been studied extensively by Ugi and
his co-workers (54,55,57,76). Ferrocene derivatives with more
than two different substituents in one ring have planar chi-
rality which cannot be described by the usual R and S nomen-
clature (58,59,77). The following modification of the nomen-
clature has been suggested by Ugi (55(b))for this type of
compound and will be used in this thesis. In Figure 9, the
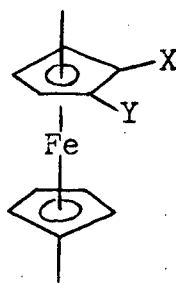
Viewed from above

Figure 9. Ferrocene derivatives with planar chirality

observer looks along th C_5 axis of the parent ferrocene rings with the disubstituted ring directed towards him. The configuration of the substituted ferrocene is termed "R" if the ligands X and Y descend in priority in the shortest clockwise arc. ("Priority" here has the same meaning as used for the usual R,S nomenclature). Likewise, if the priority ascends in a clockwise direction, the planar chirality is "S". If different types of chirality appear in one compound, e.g., X and Y contain central chiral elements, R and S symbols will refer to these various types of chirality in the order central>axial>planar. For example, in Figure 9 if X=-$C\begin{smallmatrix}CH_3\\ \,\\ NMe_2\end{smallmatrix}$ and Y=-$C\begin{smallmatrix}OH\\ \,\\ CH_3\end{smallmatrix}$ then it will be refered to as (S,R,S) (45). The first S refers to the chirality of Y which has higher priority than X which has chirality R. The third S is the planar chirality of whole molecule. If Y=$P(C_6H_5)$, as in the desired ligand, FcNP, then it is (R,S).

The preparative sequence for the chiral ferrocenylphosphine (FcNP) is sketched in Figure 10.

Both ferrocene and α-acetylferrocene are commercially available. α-Ferrocenylethanol is obtained by the reduction of α-acetylferrocene. Although Ugi (65) reported the reduction with both lithium aluminum hydride ($LiAlH_4$) and sodium bis(2-methoxyethoxy)aluminum hydride (commercially known as "Vitride"), it has been found in the present studies that Vitride is not as active as $LiAlH_4$ and chromatographic separation is required after reduction. Thus about 65% of the α-acetylferrocene is reduced by Vitride, but more than 95% reduction
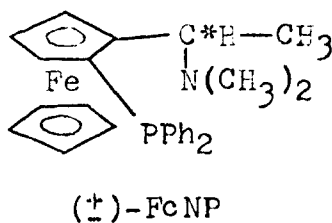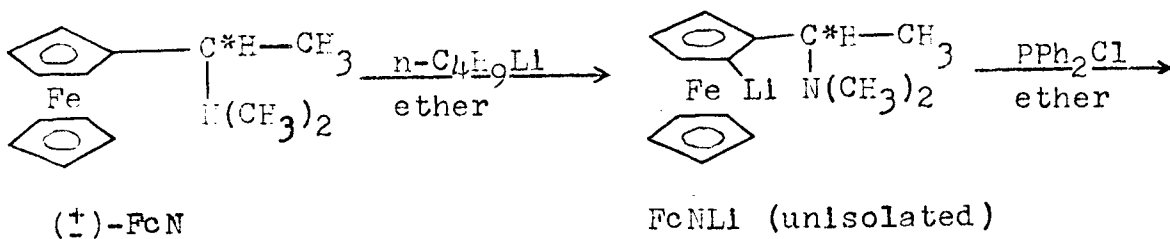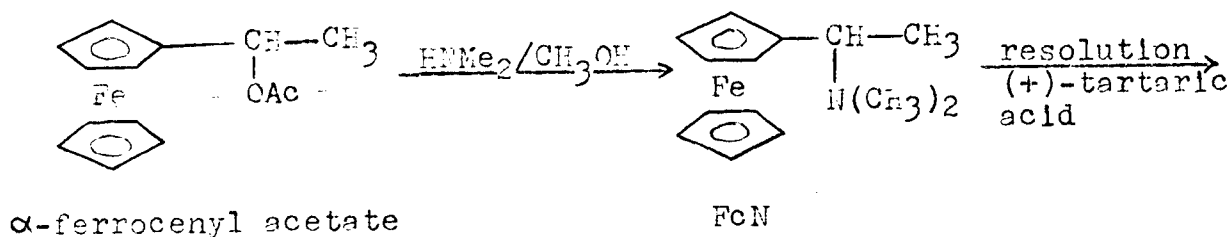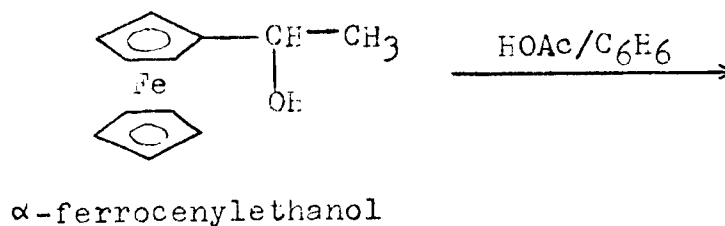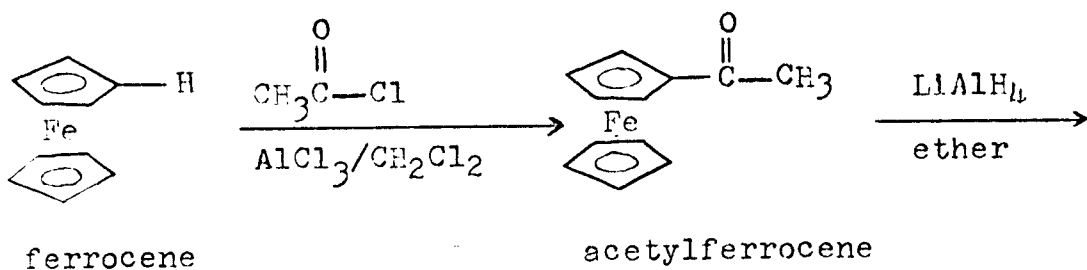
Figure 10.   Total synthesis of the chiral ferrocenylphosphine
             (+)- and (-)-FcNP.

is attained if LiAlH₄ is used. α-Ferrocenyldimethylamine is obtained by nucleophilic displacement of the acetate group by dimethylamine in aqueous methanol following treatment of α-ferrocenylethanol with acetic acid (65). Instead of getting amide and alcohol in the reaction of the carboxyate ester with the amine (78), the aminolysis proceeds with the alkylation of the amine and cleavage of the carboxylic acid. This is because the α-ferrocenylethyl carbonium ion is so stable that carboxylate anion is a sufficiently good leaving group to provide for its formation (65).

The resolution of N,N-dimethyl-α-ferrocenylethylamine with (R)-(+)-tartaric acid gives high yields of both antipodes after three recrystallizations from their respective amine tarta-rates.

Lithiation of (+)-N,N-dimethyl-α-ferrocenylethylamine ((+)-FcN) with n-butyllithium in diethyl ether-hexane as shown in a scheme on page 18 affords only the two ortho sub-stituted products, FcNLi, in a ratio of 96:4 as measured by chromatography following treatment with trimethylchlorosilane (55,63).

It was also found (76) that the major isomer reacts with anisaldehyde to give <u>8</u>. The absolute configuration of this

$$\underline{8}$$
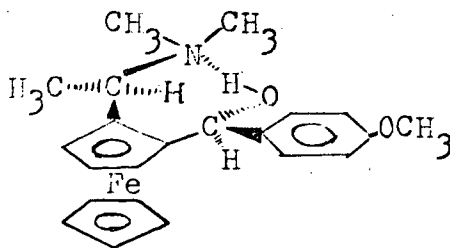
complex was determined by crystallographic techniques and the results show that the configuration about the amine-substituted carbon is R and that (+)-FcN has the R absolute configuration. Thus the marked difference between the two ortho positions with respect to lithiation apparently results from steric repulsion between the methyl group on the asymmetric carbon and the cyclopentadiene ring and also the stabilization of the lithiated derivative by coordination with the amino group. Thus lithiation of (R)-(+)-FcN affords practically pure (R,R)- FcNLi, and (S)-(-)-FcN yields practically pure (S,S)-FcNLi, the antipode of (R,R)-FcNLi. Using a more active reagent, further lithiation will occur in the unsubstituted ring (64). This second lithiation is similar to that of ferrocene itself which undergoes lithiation less readily than the amine (63,79-81). Thus Kumada et al. (81) lithiated ferrocene with n-butyllithium-N,N,N',N'-tetramethylethylenediamine (TMEDA) to give 1,1'-dilithioferrocene which was condensed with chlorodimethylphosphine to give 1,1'-bis(dimethylphosphino)- ferrocene and has been used to prepare metal complexes (81).

In the present investigation the diphenylphosphino derivative of ferrocenylethylamine was formed by the reaction of FcNLi with chlorodiphenylphosphine in ether. The resulting mixture was hydrolyzed by adding an aqueous slurry of sodium bicarbonate and the product was extracted into the ether phase. The ferrocenylphosphine-ether phase was carefully dried with MgSO4 and, after evaporating the solvent, the pro- duct was obtained as brown yellow solid which was recrystal-

lized from ethanol three times to afford crystalline phos-
phine in a yield about 35%. At about the same time this work
was initiated an independent identical synthesis of the same
ligand by Japanese workers was described (64). They isolated
the phosphine by alumina-column chromatography and purified
it by recrystallization from ethanol (50%).

Figure 11 shows the absolute crystallographic structure
of (S,R)-FcNP (95). Significant features about the structure
are as follows: (i) the methyl group on the asymmetric carbon
is directed away from the cyclopentadiene ring; this confirms
the absolute configuration of the starting amine discussed
before (p. 41); (ii) the cyclopentadiene rings are eclipsed
whereas in parent ferrocene they are staggered.

Synthesis of Metal Complexes of the FcNP Ligand

Some initial attempts to prepare complexes of FcNP with
compounds of Ni, Pt and Pd were largely unsuccessful. The only
well characterized products, apart from the cationic rhodium
complexes to be described next, were $(FcNP)Ni(CO)_3$ and $(FcNP)$-
$Rh(CO)Cl$. The former was obtained by direct reaction of the
ligand with $Ni(CO)_4$ in diethyl ether solution.

$$FcNP + Ni(CO)_4 \longrightarrow (FcNP)Ni(CO)_3 + CO$$
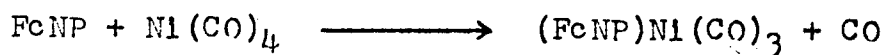
This complex which was characterized by microanalysis,
shows IR absorption of carbonyl groups at 1980, 2000 and 2060
cm^{-1}. Most $Ni(CO)_3$ complexes show only two such bands so ap-
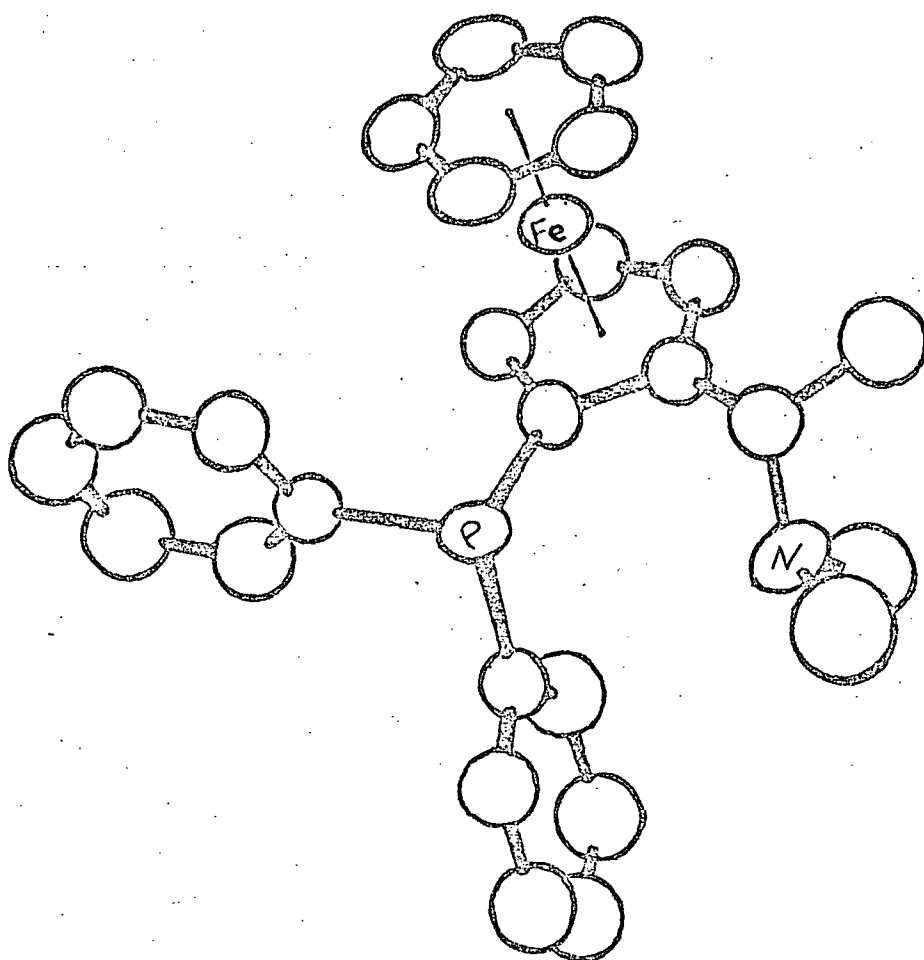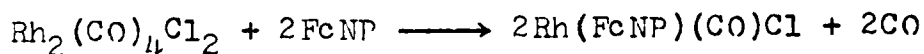parently the bulky FcNP coordinated to the nickel destroys

Figure 11.   Absolute crystallographic structure of
            (S,R)-FcNP (95).

the local C_{3v} symmetry.

The complex Rh(FcNP)(CO)Cl was obtained by reacting Rh$_2$(CO)$_4$Cl$_2$ with FcNP in benzene. The IR spectrum shows one

$$Rh_2(CO)_4Cl_2 + 2FcNP \longrightarrow 2Rh(FcNP)(CO)Cl + 2CO$$

carbonyl absorption band at 1990 cm^{-1}. This compound crystallizes with one benzene molecule of solvation as indicated by microanalysis and the NMR spectrum. In the free ligand, the chemical shift of the N-methyl hydrogens is 1.80 ppm (singlet); but the complex shows two absorptions (2.47 and 3.14 ppm) of the equal area. Thus in this complex FcNP acts as a bidentate ligand with both N and P coordinated to the rhodium. The chloride and carbonyl group are cis to each other. Although Rh(PPh$_3$)$_2$(CO)Cl has the trans configuration, it is not unusual to find the cis Rh(CO)Cl moiety in chelate derivatives (P-P)Rh(CO)Cl ((P-P) = Ph$_2$P(CH$_2$)$_2$PPh$_2$ (82), Ph$_2$P$\overline{\text{C=CPPh}_2(\text{CF}_2)_4}$ (83)).

The general methods of synthesis of the ionic rhodium complexes are based on the published methods (74) with minor modifications. These preparative sequences are summarized in Figure 12. The preparation of the optically active complexes simply involved the same procedures but optically active FcNP was used instead of racemic FcNP.

The equivalent conductivities of four of the compounds, [(COD)Rh(FcNP)]$^+$BF$_4^-$, [(NBD)Rh(FcNP)]$^+$PF$_6^-$, [(COD)Rh(FcNP)]$^+$ClO$_4^-$ and [(COD)Rh((-)-FcNP]$^+$BPh$_4^-$ have been measured. All these

$$[Rh(NBD)Cl]_2 \begin{cases} \xrightarrow[C_6H_6/THF]{FcNP, \ NH_4PF_6} [(NBD)Rh(FcNP)]^+PF_6^- \\ \\ \xrightarrow[C_6H_6/THF]{FcNP, \ NaClO_4} [(NBD)Rh(FcNP)]^+ClO_4^- \end{cases}$$

$$[Rh(COD)Cl]_2 \begin{cases} \xrightarrow[(C_2H_5)_2O]{acetylacetone} (acac)Rh(COD) \\ \\ \xrightarrow[FcNP/THF]{HClO_4} [(COD)Rh(FcNP)]^+ClO_4^- \\ \\ \xrightarrow[C_2H_5OH]{FcNP, \ NH_4BF_4} [(COD)Rh(FcNP)]^+BF_4^- \\ \\ \xrightarrow[CH_2Cl_2]{FcNP, \ NaPF_6} [(COD)Rh(FcNP)]^+PF_6^- \\ \\ \xrightarrow[CH_3OH]{FcNP, \ NaBPh_4} [(COD)Rh(FcNP)]^+B(C_6H_5)_4^- \end{cases}$$
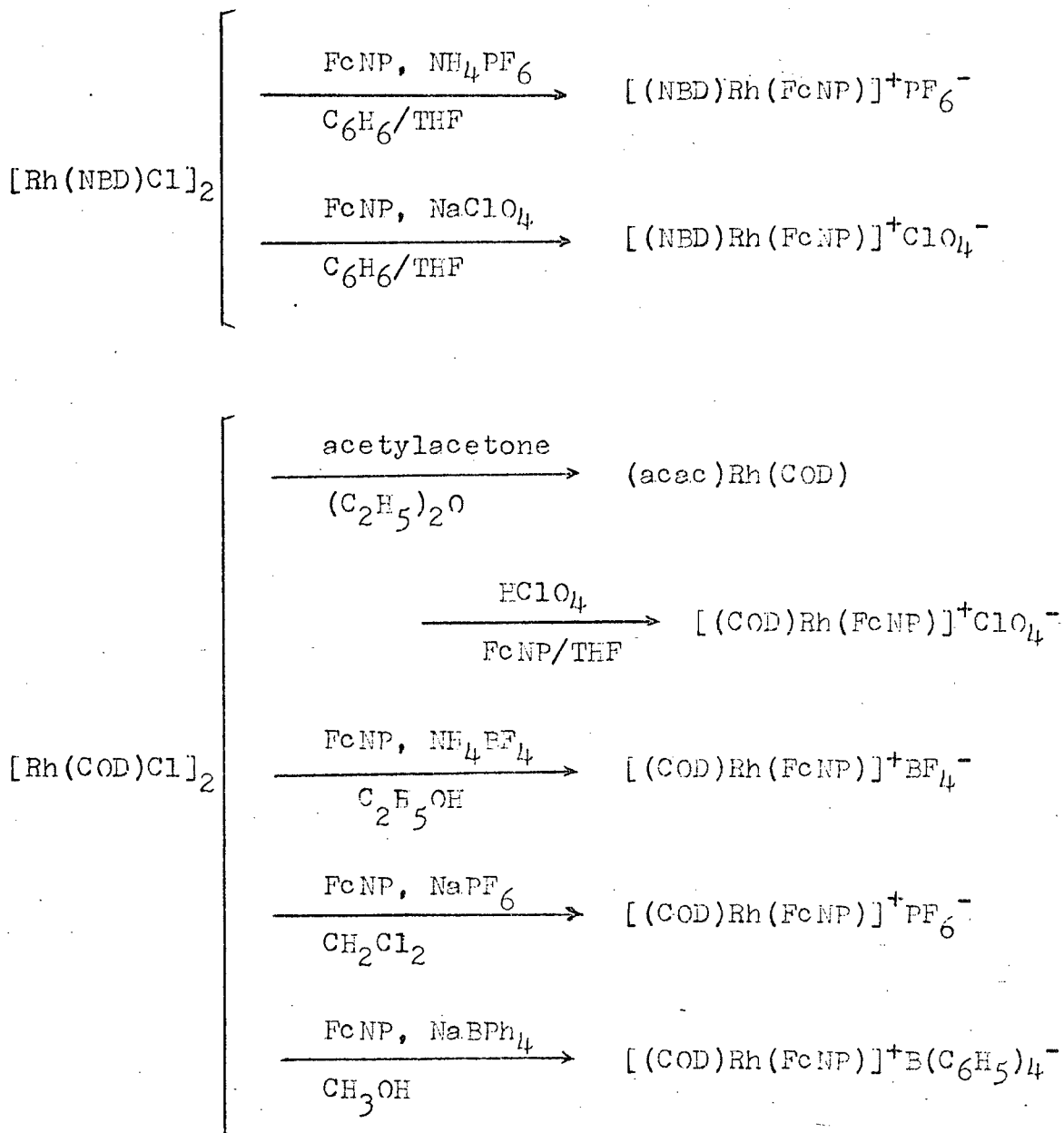
Figure 12. Preparation of ionic rhodium complexes with the FcNP ligand.

are in the range of 74 ohm^{-1}cm^{-1}M^{-1} except one ([(COD)Rh((-)-FcNP)]$^+$BPh$_4^-$), which is 50.13 ohm^{-1}cm^{-1}M^{-1}.

The NMR spectrum of [(NBD)Rh(FcNP)]$^+$PF$_6^-$ shows that the amino group of FcNP is coordinated to the metal with two absorptions due to the N-methyl hydrogens at 2.42 and 3.19 ppm, compared with the singlet of the free ligand at 1.80 ppm. In the case of [(COD)Rh(FcNP)]$^+$BF$_4^-$, the two bands due to the methyl groups are found at 2.71 and 3.30 ppm. The NMR data as well as the elemental analysis suggested that only one FcNP ligand per rhodium is found in all the ionic complexes even though attempts to prepare complexes with two FcNP ligands per rhodium were made by using excess ligand.

Asymmetric Homogeneous Hydrogenations

(I). Catalytic Precursors and Catalytic Principles

In the previous section, the preparation and some properties of the catalyst precursors, [(diene)Rh($\pm$)-FcNP]$^+$A$^-$ (A$^-$: PF$_6^-$, BF$_4^-$, ClO$_4^-$ and B(C$_6$H$_5$)$_4^-$), have been described. Here the word "precursor" is used because it has been well-documented (86) that cation complexes [(diene)RhL$_n$]$^+$A$^-$ (diene: norbornadiene or 1,5-cyclooctadiene; A$^-$: PF$_6^-$, BF$_4^-$ or ClO$_4^-$; L: a tertiary phosphine, arsine (n=2 or 3) or a chelating di-(tertiary phosphine) (n=1)), react readily with molecule hydrogen (1 atm, 25°) in solution (acetone or alcohol); diene is quantitatively reduced to alkane and catalytically active

complexes of formula $[RhL_nH_2]^+$ are thereby generated in situ. This kind of catalyst precursor offers several notable advantages over the in situ prepared Wilkinson type catalysts. Some are as follows: (i) the complexes can be prepared and isolated easily; (ii) the diene is completely reduced and eliminated from the coordination sphere of rhodium; thus a vacancy is left for the binding of hydrogen and the substrate to be reduced; (iii) the reaction pathway does not involve dissociation of a ligand and thus the reactions are much less solvent dependent.

In the present work it has been observed that in alcoholic solutions, $[(diene)Rh((\pm)-FcNP)]^+$ reacts with hydrogen (1 atm, $32°$) in the absence of substrate. The bright yellow color fades to pale yellow in a few minutes; this is presumably due to the formation of $[Rh((\pm)-FcNP)H_2S_x]^+$, where S is the solvent.

(II). Catalytic Hydrogenation of Olefins

Knowles and co-workers (33) reported that active catalytic solutions can be prepared in situ by mixing $[(1,5-hexadiene)-RhCl]_2$ or even $RhCl_3 \cdot 3H_2O$ with chiral ligands, L*, in alcoholic solution and the results are identical with these obtained using the crystalline complexes $[(COD)RhL*_2]^+B(C_6H_5)_4^-$ or BF_4^-. However, in the present study, it was decided to use the well-characterized complexes $[(diene)Rh(\pm)-FcNP]^+A^-$ to catalyze the hydrogenation of olefins.

The prochiral substrates which were investigated are

listed in Figure 13. The extent of reaction was monitored using a simple gas uptake apparatus and was checked by determining the NMR spectrum of the final reaction products. Table 2 and 3 show the results obtained for the homogeneous hydrogenation of α-acetamidocinnamic acid and α-acetamidoacrylic acid respectively, using cationic chiral Rh-FcNP complexes as catalyst precursors. High optical yields are obtained in the case of α-acetamidocinnamic acid and the results seem to be independent of the diene as expected. The anion except for $B(C_6H_5)_4^-$ plays little role on the optical yield although it seems that catalyst precursors with ClO_4^- or PF_6^- as anion give faster rates. The use of $B(C_6H_5)_4^-$ as counterion in rhodium complexes has been discussed by Osborn (84) and Bennett(85). They found that one of the arene rings of the tetraphenylborate coordinates to the metal via a h^6 interaction to form a complex shown as 2, where L is triphenyl-

$$\begin{array}{c} \bigcirc\!\!\!\!\!\bigcirc\!\!-\!\!\overset{-}{B}(C_6H_5)_3 \\ | \\ Rh^+ \\ \diagup \ \diagdown \\ L \qquad L \end{array}$$
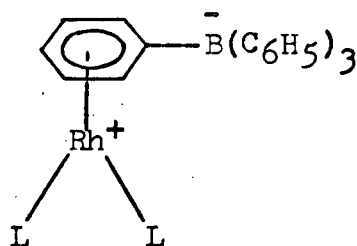
2

phosphine, following hydrogen treatment of the cationic complex in solution. A similar h^6 interaction of one arene ring
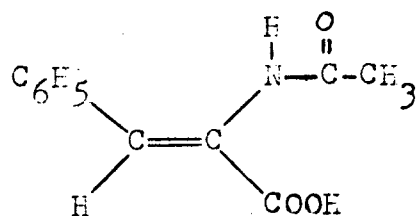
α-Acetamidocinnamic Acid*
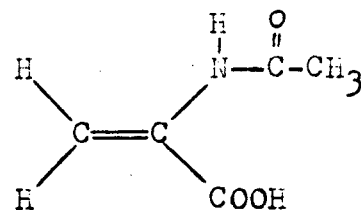
α-Acetamidoacrylic Acid*
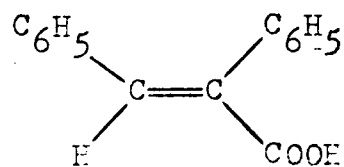
α-Phenylcinnamic Acid
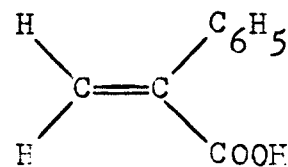
Atropic Acid

α-Methylcinnamic Acid

β-Methylcinnamic Acid

* These two substrates have been most intensively studied because they belong to a class of compounds which are amino acid precursors.

Figure 13. Prochiral α,β-unsaturated carboxylic acid substrates used in this study.

Table 2. Asymmetric Hydrogenation of α-Acetamidocinnamic Acid with the FcNP-Rh Catalyst[a].

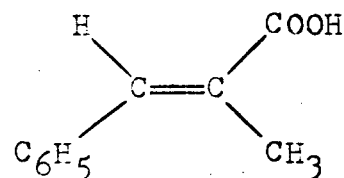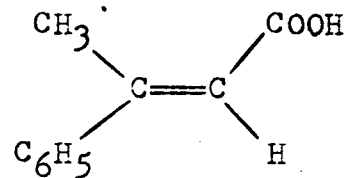| Catalyst precursor	Solvent	Time (hr)	Conversion (%)	Optical yield (%)[b]	Configuration
[(COD)Rh((-)-FcNP)]ClO$_4$	methanol	25	91	80	S
[(COD)Rh((+)-FcNP)]ClO$_4$	methanol	25	93	73	R
[(COD)Rh((-)-FcNP)]BF$_4$	ethanol	40	83	75	S
[(NBD)Rh((-)-FcNP)]ClO$_4$	methanol	25	93	78	S
[(COD)Rh((÷)-FcNP)]BF$_4$	ethanol	48	91	83	R
[(NBD)Rh((+)-FcNP)]PF$_6$	isopropanol	48	96	80	R
[(NBD)Rh((+)-FcNP)]PF$_6$	ethanol	22	88	84	R
[(COD)Rh((-)-FcNP)]B(C$_6$H$_5$)$_4$	methanol	-[c]	-[c]	-[c]	-[c]

[a]Reactions were carried out at 1 atm H$_2$ and 32°. The concentration of the catalyst was 1.0×10^{-3} M and the substrate 1.0×10^{-1} M. [b]Optical yields are calculated on the basis of reported values for the optically pure compounds: N-acetyl-(R)-phenyl-alanine, $[\alpha]_D^{26}$ -51.8 (c 1, EtOH) (92); N-acetyl-(S)-phenylalanine, $[\alpha]_D^{26}$ +46.0 (c 1, EtOH) (93). [c]The reaction rate was too low to be measured.

Table 3. Asymmetric Hydrogenation of α-Acetamidoacrylic Acid with the FcNP-Rh Catalyst[a].

Catalyst precursor	Solvent	Time (hr)	Conversion (%)	Optical yield (%)[b]	Configuration
[(COD)Rh((−)-FcNP)]BF$_4$	methanol	7	100	58	S
[(COD)Rh((+)-FcNP)]ClO$_4$	methanol	7	100	55	R
[(COD)Rh((−)-FcNP)]ClO$_4$	methanol	6	100	43	S
[(COD)Rh((−)-FcNP)]B(C$_6$H$_5$)$_4$	methanol	92	90	26	S

[a]Reactions were carried out at 1 atm H$_2$ and 32°C. The concentration of the catalyst was 1.0×10^{-3} M and the substrate 1.0×10^{-1} M. [b]Optical yields were calculated on the basis of reported value for the optically pure compound: N-acetyl-(R)-alanine, $[\alpha]_D$ +66.5 (c 2, H$_2$O) (94); the pure (S)-isomer was assumed to have the same degree of optical rotation with opposite direction.

with the metal may happen in the present instance after $[(COD)Rh((-)-FcNP)]^+BPh_4^-$ reacts with hydrogen. The rate of hydrogenation of α-acetamidoacrylic acid using $[(COD)Rh-((-)-FcNP)]^+BPh_4^-$ as the catalyst is about one-thirteenth the rate of that when the anion is BF_4^-; and the optical yield of N-acetylalanine is half the value when $[(COD)Rh((-)-FcNP)]^+BF_4^-$ is used as the catalyst (see Table 3). Also, when $[(COD)Rh-((-)-FcNP)]^+BPh_4^-$ was used to catalyze the hydrogenation of α-acetamidocinnamic acid, the reaction rate was so low that no hydrogen uptake was detected. In contrast, Knowles and co-workers found that $[(COD)Rh((\pm)-ACMP)_2]^+B(C_6H_5)_4^-$ is as good a catalyst as the same cation used with BF_4^- or PF_6^- as the anion at 3.7 atm (75) and 0.7 atm (33). It is difficult to account for the differences.

In the case of the cationic rhodium complexes it seems that the composition of the solvent is not an important variable in determining the hydrogenation reaction rate and product optical purity (75), and in the present study, methanol, ethanol and isopropanol were used. In contrast, in a study of Wilkinson type catalysts, Masler (38) showed that solvent composition of benzene-ethanol (1:1, v/v) gives the best results (high chemical and optical yields) when $[(+)-NMDPP]_3RhCl$ is used to catalyze the hydrogenation of (E)-α-methylcinnamic acid. When the ratio was changed to 3:1 (benzene-ethanol), only 83% is reduced, and the optical yield is 2% lower (compared with 100% reduction in 24 hours if 1:1 benzene-ethanol solvent is used). If pure benzene is used,

only 13% reduction after 24 hours is achieved; and in 2-butanone, reduction takes place to the extent of 40% and the optical purity of the product drops to 26.5% e.e. from 60% e.e. obtained in 1:1 benzene-ethanol. The results are summarized in Table 4.

Table 3 shows that the reaction rates for the hydrogenation of α-acetamidoacrylic acid are about four times faster than the rates for the hydrogenation of α-acetamidocinnamic acid (see Table 4), but the optical yields of N-acetylalanine produced are much lower. Again, $[(COD)Rh(-)-FcNP]^{+}B(C_6H_5)_4^{-}$ is peculiar with regard to both reaction rate and optical yield; thus it takes 92 hours to achieve 95% hydrogenation (estimated from the NMR spectrum) and the optical yield is only 26%.

In the hydrogenation of both α-acetamidocinnamic acid and α-acetamidoacrylic acid, catalysts with (+)-FcNP as the ligand always give products with the R configuration whereas catalysts with (-)-FcNP give the S configuration. Earlier, Kagan and Sinou (46) postulated the reaction intermediate shown as 5 (p.16) to account for the results of many homogeneous catalytic hydrogenations of -acylamidoacrylic acids using DIOP as the asymmetric ligand. The major feature is that the acetyl oxgen atom as well as the double bond is coordinated to the rhodium. This ensures that the olefin is held in a rigid orientation so that when the hydrogen on the rhodium is transfered to the prochiral carbon atom in the next step of the reaction, it is transferred stereospecifically.

Table 4. The Influence of Solvents on the Reduction of (E)-α-Methylcinnamic Acid
by the Rhodium-(+)-NMDPP Catalyst System (38).

Solvent	Reduction (%)	Yield (%)	Configuration	Optical yield (%)
1:1 benzene-ethanol	100	90.3	R	60.0
3:1 benzene-ethanol	83	67.0	R	58.0
benzene	13	-	-	-
2-butanone	40	-	R	26.5
1:1 benzene-ethanol[a]	100	71.0	R	56.3

[a]In this experiment 25 mmole of substrate and 25 mmole of triethylamine were used.

In one experiment (88) an _in situ_ catalyst prepared from $[(C_2H_4)_2 RhCl]_2$ and (+)-DIOP was used to catalyze the hydrogenation of N-acetyl-α-phenyl ethylamine in both ethanol and benzene as solvents. Both the reactions gave about the same optical yields (42.5 and 44% respectively) but different configurations were obtained. This phenomenon was ascribed to a change of mechanism (87); the argument being that in pure benzene the enamide would be coordinated to rhodium only by its double bond. In the presence of alcohol, dissociation of Rh-Cl bond could occur to give a cationic species which would then interact with both the double bond and the amide group of the enamide.

Intermediates of the type shown as 5 can also be used to explain the results obtained during the present investigation. On this basis two intermediates can be drawn as in Figure 14 and Figure 15 when (R,S)-(-)-FcNP is the ligand. The diene (NBD or COD), which was coordinated to the metal, has reacted with hydrogen to form the alkane and has left the coordination sphere. The vacant sites are occupied by the substrate which forms both a metal---olefin bond and a metal---amide bond.

The two faces of the substrate double bond are specified as follows: when the substrate molecule is drawn as 10, then
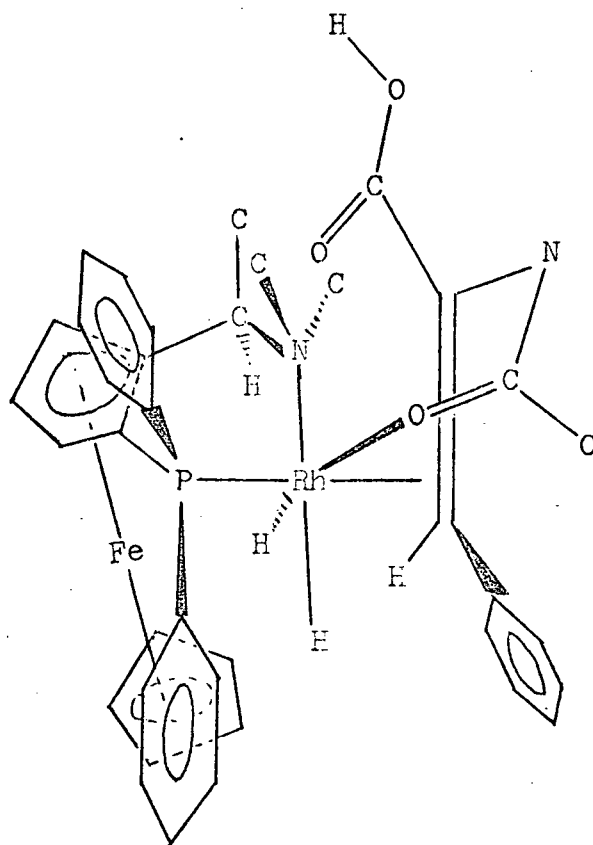

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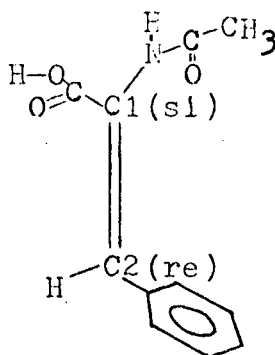
Figure 14. A proposed intermediate in which the si-re face of the substrate is directed towards the metal complex with (R,S)-FcNP as the ligand.
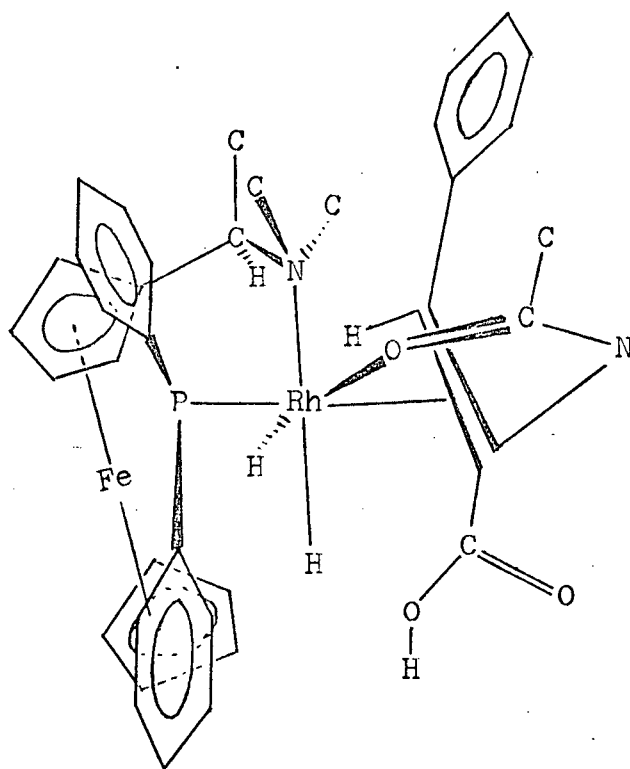
Figure 15. A proposed intermediate in which the re-si face of the substrate is directed towards the metal complex with (R,S)-FcNP as the ligand.

"si" is assigned (89) to the face around C1 according to the usual priority rule, and "re" is assigned to the face around C2 (when viewed from above the page). The face facing the viewer is called the si-re face.

In Figure 14 the si-re face of the substrate is directed towards the metal and three steric repulsions are apparent: one is the repulsion between the phenyl groups of the substrate and the ligand; the second is between the phenyl group of the substrate and the cyclopentadiene ring; the third is between the carboxylic group and the methyl groups on the ligand nitrogen.

In the case shown in Figure 15 in which the re-si face of the substrate approaches the catalyst, these steric repulsions are minimized.

From this analysis it can be seen that hydrogen transfer to the coordinated olefin in the more favored case (Figure 15) will give a product with the S configuration.

When (S,R)-(+)-FcNP is considered, the more stable intermediate which can be constructed is the mirror image of the intermediate shown in Figure 15. This will afford products of configuration R.

When the substrate is α-acetamidoacrylic acid, similar intermediates can be constructed. However, since the phenyl group is replaced by a hydrogen atom, the only stereochemical control is the repulsion between the carboxylic group on the substrate and the methyl groups on the ligand nitrogen. This accounts for the results that Rh-(+)-FcNP complexes still give

products predominantly with configuration R and Rh-(-)-FcNP
complexes give predominantly S; but with lower optical yield.

Table 5 lists the results Knowles et al. obtained (30,34)
when different α-acylamidoacrylic acids were hydrogenated
using cationic rhodium complexes with $\underline{3}$ as the ligand. It is
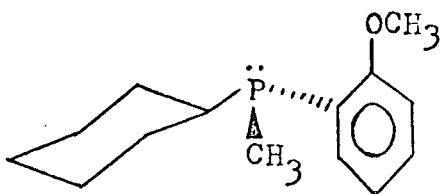
(+)-(R)-ACMP $\underline{3}$

seen that higher optical yields are obtained if R_1 is a bulky
substituent. In this case the methoxy group on the ligand
is believed to form a hydrogen bond with the amide group of
the coordinated substrate, which would account for the ste-
reochemical control (34). It seems unlikely that an inter-
mediate of the type shown in Figure 15 would account for the
results since two separate phosphines would not give the ste-
ric bulk associated with the size and rigidity of the chelated
FcNP ligand.

In the present investigation, attempts to hydrogenate
four other substrates: atropic acid, α-phenylcinnamic acid,
and α-, β-methylcinnamic acids were made using [(COD)Rh(+)-

Table 5. Asymmetric Hydrogenation of α-Acylamidoacrylic Acids by Rh-complex with o-Anisylcyclohexylmethylphosphine as the Ligand (30).

$$R_1 \diagdown C = C \diagup \begin{matrix} COOH \\ NHCOR_2 \end{matrix} \quad \longrightarrow \quad R_1 CH_2 - \overset{COOH}{\underset{NHCOR_2}{C}} - H$$

R_1	R_2	Optical yield (%)	Resulting amino acid
$3\text{-MeO-4-OH-}C_6H_3$	Ph	90	L-DOPA
$3\text{-MeO-4-OH-}C_6H_3$	Me	88	L-DOPA
C_6H_5	Me	85	L-phenylalanine
C_6H_5	Ph	85	L-phenylalanine
$p\text{-Cl-}C_6H_4$	Me	77	p-chloro-L-phenylalanine
3-(1-Ac-indolyl)	Me	80	L-tryptophan
H	Me	60	L-alanine

FeNP]$^+$BF$_4$$^-$ as the catalyst precursor. No hydrogen uptake was observed after two days. A possible explanation is that these prochiral olefins lack the amide group which, in the presence of the bulky FcNP ligand, is indispensable to bind the substrate before hydrogen transfer. This pattern is also found in the cationic rhodium catalyst using ACMP 3 as the ligand (75), where simple olefins are reduced at a rate about one-tenth the rate of α-acetamidocinnamic acid (Table 6).

A similar ligand, (S,R)-BPPFA, 11 (64) has been used to

11

produce a catalyst in situ for the hydrogenation of α-acylamidoacrylic acids at 50 atm hydrogen presure and room temperature (90). The results are shown in Table 7. In this case it was postulated that attractive interaction between an uncoordinated amino group on the ligand and the carboxylic group on the substrate contributes to the asymmetric induction. However, in view of the present results, the amino group could be expected to coordinate to rhodium and thus the reaction intermediate could be similar in structure to that suggested above for the FcNP complexes.

Table 6. Hydrogenation Rates of Various Olefins Catalyzed by
Rh-DIOP and Rh-ACMP complexes (31,32,75)

Catalyst ligand	Substrate	Approx. rel. rate
ACMP	α-acetamidocinnamic acid	1
DIOP	α-acetamidocinnamic acid	2
ACMP	cyclooctadiene	<.1
ACMP	norbornadiene	.5
ACMP	1-octene	.5
ACMP	α-phenylacrylic acid	<.1

Table 7. Asymmetric Hydrogenation Catalyzed by (S,R)-BPPFA-Rh
Complex[a] (90).

Olefin	Solvent	Optical yield (%) (Configuration)
PhCH=C(NHCOMe)COOH	MeOH	93 (S)
	H_2O/EtOH (1/1)	92 (S)
	H_2O/MeOH (1/1)	89 (S)
AcO-⬡-CH=C(NHCOMe)COOH	MeOH	8 (S)
	EtOH	38 (S)
MeO / AcO-⬡-CH=C(NHCOMe)COOH	H_2O/MeOH (1/3)	87 (S)
	EtOH	36 (S)
⬡-CH=C(NHCOMe)COOH	H_2O/MeOH (1/2)	86 (S)
	H_2O/MeOH (3/4)	52 (S)

[a] $P(H_2)$ = 50 atm; (S,R)-BPPFA/Rh = 1.2/1; Rh/Substrate = 0.5 mol%.

GENERAL CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE WORK

The most important finding of this work is that the chiral Rh-FcNP complexes catalyze the hydrogenation of a class of compounds which are amino acid precursors in high optical yield and under mild conditions ($32°$ and 1 atm H_2). The highest optical yield is 84% which is comparable to the best results (85%) obtained with a Rh-ACMP complexes and is better than the results (72%) obtained with a Rh-DIOP complexes as catalyst.

The ligand is fairy easily to prepare (about ten steps from the starting material to both (+)- and (-)-FcNP) and to isolate in optically pure form and the complexes $[(diene)Rh-(\pm)-FcNP]^+A^-$ which can be isolated in crystalline form are believed to be the catalyst precursors.

When the Rh-FcNP complexes are used to catalyze the hydrogenation of α,β-unsaturated acids, the rate is found to be very low. It seems that the present catalytic system is good for the hydrogenation of α-acylamidoacrylic acids and, if the proposed intermediate is correct, other enamides.

There are many directions for further work in the area of asymmetric reactions in which the catalyst contains asymmetric ligands which are ferrocene derivatives. One would be to modify both rings of ferrocene to obtain ligands with more than two donor sites. An example was prepared recently (64) as follows:

$$\text{Fc} \begin{array}{c} \text{—C*H(CH}_3\text{)N(CH}_3\text{)}_2 \\ \text{PPh}_2 \end{array} \quad \xrightarrow[\text{b) PPh}_2\text{Cl}]{\text{a) n-BuLi}} \quad \text{Fe} \begin{array}{c} \text{—C*H(CH}_3\text{)N(CH}_3\text{)}_2 \\ \text{PPh}_2 \\ \text{PPh}_2 \end{array}$$
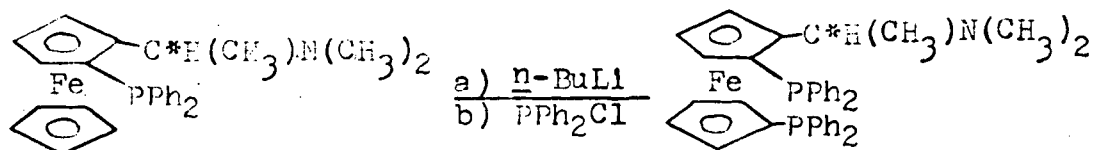
This could coordinate to metals using the two phosphorus atoms leaving the amino group free to interact with the bound substrate.

A similar procedure could yield a vinyl group on the second ring to give a derivative which could be polymerized to yield an optically active polymeric ligand which could be used in supported catalyst systems.

Other reactions such as hydrosilylation are catalyzed by Rh complexes and complexes of ligand such as FcNP should be investigated with respect to the addition of Si-H to C=C, C=O, and C=N bonds. In addition, the asymmetric hydrogenation of C=O and C=N bonds should be studied.

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