Durham E-Theses

Studies of the catalysis of cyanide addition and substitution

Hodgson, Martin

STUDIES OF THE CATALYSIS OF CYANIDE ADDITION

AND SUBSTITUTION

Martin Hodgson, B.Sc. Hons. (Dunelm)

(College of St. Hild and St. Bede)

University of Durham

Thesis presented for the degree of Doctor of Philosophy

September 1988.

DECLARATION

The work described in this thesis was carried out in the
Chemistry Department of the University of Durham and at
W.R. Grace, Seal Sands between October 1983 and September 1986.
Except where acknowledged by reference, this is the original
work of the author and has not been submitted for any other
degree.

Parts of this work were presented as a poster at the Royal Society of Chemistry 3rd International Conference on "The Chemistry of the Platinum Group Metals", University of Sheffield, 12-17 July 1987.

ABBREVIATIONS

Ac	Acetyl.
BINAP	2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl.
BOC	Tert-butoxycarbonyl.
BPPM	(2S,4S)-N-(tert-Butoxycarbonyl)-4-(diphenylphosphino)-2-[(diphenylphosphino)methyl]-pyrrolidine.
dba	Dibenzylideneacetone
DIOP	2,3-O-Isopropylidene-2,3-dihydroxy-1,4-bis(diphenyl-phosphino)butane.
DIPAMP	1,2-Bis-(o-methoxyphenylphenylphosphino)ethane.
DMSO	Dimethylsulphoxide
DPMPH	Diphenylmenthylphosphinite.
e.e.	Enantiomeric excess.
I.R.	Infra Red.
N.M.R.	Nuclear Magnetic Resonance.
PNP	See page 50.
THF	Tetrahydrofuran.
TMS	Trimethylsilyl in Chapter 4, Tetramethylsilane elsewhere.
U.V.	Ultra-violet.

ABSTRACT

STUDIES OF THE CATALYSIS OF CYANIDE ADDITION AND SUBSTITUTION

By MARTIN HODGSON

The chiral diphenylphosphinites of menthol and binaphthol have been prepared. The zerovalent palladium complexes of these phosphinites were found to be poor catalysts for the hydrocyanation of alkenes.

The enantiomeric purity of the exo-norbornane carbonitrile produced from the hydrocyanation of norbornene catalysed by Pd(DIOP)$_2$ was found to be considerably lower than originally surmised. In the same reaction, the zerovalent palladium complexes of BPPM and BINAP were found to give the highest reported enantiomeric purities for a transition metal catalysed hydrocyanation reaction.

The mechanism of transition metal catalysed asymmetric hydrocyanation was examined. Preliminary mechanistic investigations were conducted using (DIOP) platinum(0) alkene complexes. The formation of a platinum hydrido cyanide complex was observed by ^{i}H and ^{31}P N.M.R. spectroscopy. The novel complex (DIOP) palladium(0) ethene has been prepared and isolated, yielding the first crystal structure of a palladium ethene complex. Oxidative addition of HCN to the complex generated (DIOP) palladium hydrido cyanide. The complex also underwent other oxidative addition reactions; some may involve one electron processes.

The use of PNP salts to effect the introduction of CN$^-$ by addition or substitution reactions is described. The salts are particularly suited to reactions with hydrolysis sensitive substrates. The salts are used under both phase transfer and stoichiometric conditions.

To my parents and friends.

CONTENTS

CHAPTER 1

STUDIES OF THE CATALYSIS OF CYANIDE ADDITION AND

SUBSTITUTION - INTRODUCTION

1.1. INTRODUCTION

The existence of organic chemistry, and the uniqueness of carbon in forming an unimaginably vast range of compounds, is due to the fact that not only are carbon to carbon bonds very strong, but also that they retain their strength when the carbons are bonded to other elements. The carbon skeleton of a molecule determines many of its physical and chemical properties, and constitutes the framework which supports the other elements making up functional groups. Therefore, carbon-carbon bond formation is the most important reaction in organic chemistry, and both the control and efficiency of bond formation is desirable. The ideal carbon-carbon bond forming reaction should be not only regioselective, but also enantioselective and catalytic.

The introduction of cyanide functionality into a molecule is attractive, as nitriles are versatile synthetic intermediates, which may be hydrolysed to carboxylic acids or reduced to primary amines (Scheme 1). Most carbon-carbon bond forming reactions involve the attack of nucleophilic carbon centres on the more electrophilic carbon centres present in, for example, carbonyl compounds and alkyl halides.

Carbon nucleophiles include cyanides, acetylides and enolates. Grignard and alkyllithium reagents are polarized so that the carbon bonded to the metal is nucleophilic. They react with aldehydes and ketones to give alcohols, or with carbon dioxide giving carboxylic acids. Their use is limited by their strong basicity which promotes elimination reactions.

Cycloadditions such as the Diels-Alder reaction also form

$$RCN \xrightarrow{H^+, \ H_2O} RCO_2H$$

$$RCN \xrightarrow{OH^-} RCO_2^-$$

$$CH_3CH_2CH_2CN \xrightarrow[\text{2 } H_2O]{\text{1 } LiAlH_4} CH_3CH_2CH_2CH_2NH_2$$

$$\text{Ph}-CH_2CN \xrightarrow[140°C]{H_2 \ , \ Ni} \text{Ph}-CH_2CHNH \longrightarrow \text{Ph}-CH_2CH_2NH_2$$
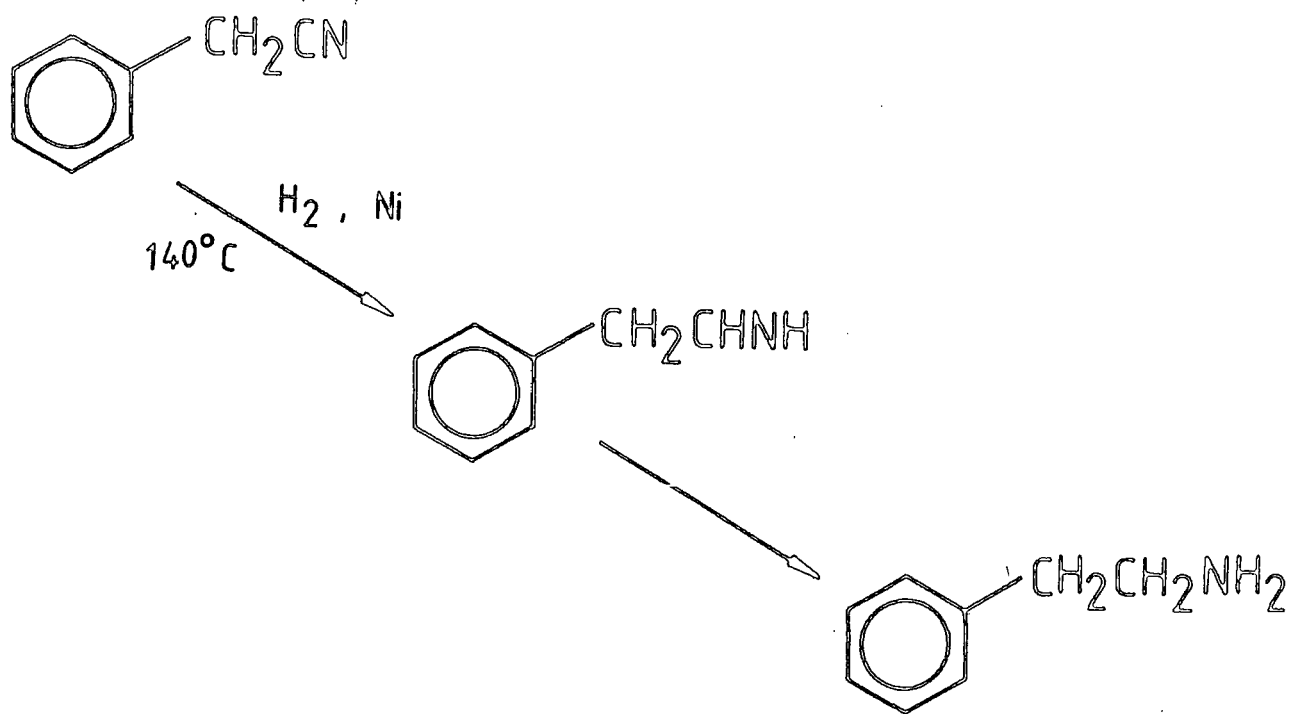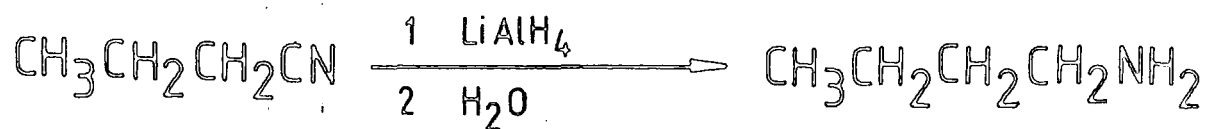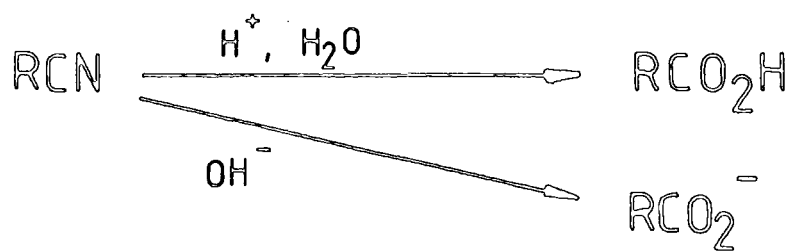
SCHEME 1.

C-C bonds with great specificity, but they require relatively complicated starting materials such as a cis 1-3 diene and an electron-deficient alkene. Organometallic complexes, of which a Grignard reagent is a simple example, can be used to effect many types of carbon-carbon bond forming processes, with great stereo- and regioselectivity. The disadvantage, particularly of organotransition metal complexes, can be their high cost. This is often offset by high catalytic efficiency, requiring only small amounts of the metal catalyst. The different types of carbon-carbon bond forming reactions involving metal complexes have been classified by Semmelhack [1] (Scheme 2).

This project is concerned with two carbon-carbon bond forming reactions.

(i)   HYDROCYANATION. Although homogeneous transition metal catalysed hydrocyanation has been known for over twenty years, asymmetric hydrocyanation has been little studied. The mechanism of transition metal catalysed hydrocyanation has also received little attention.

(ii)   REACTIONS OF THE CYANIDE ION IN AN ORGANIC PHASE. The reactions of the cyanide ion can be enhanced and modified by the use of quaternary ammonium salts. The synthetic utility of triphenyl(P,P,P-triphenyl-phosphine imidato-N)phosphorus, (PNP) salts in such reactions, under both phase transfer and stoichiometric reaction conditions has been investigated.

$R_2M(II) \longrightarrow R-R + M(0)$ REDUCTIVE ELIMINATION

$R-M-C=X \longrightarrow R-\underset{X}{\overset{}{C}}-M$ α- INSERTION

$R-M-\| \longrightarrow R\diagup\diagdown M$ β - INSERTION

$\|-M-C=X \longrightarrow$ CYCLOINSERTION

$\|-M-\| \longrightarrow$ CYCLOADDITION

NUCLEOPHILIC
SUBSTITUTION
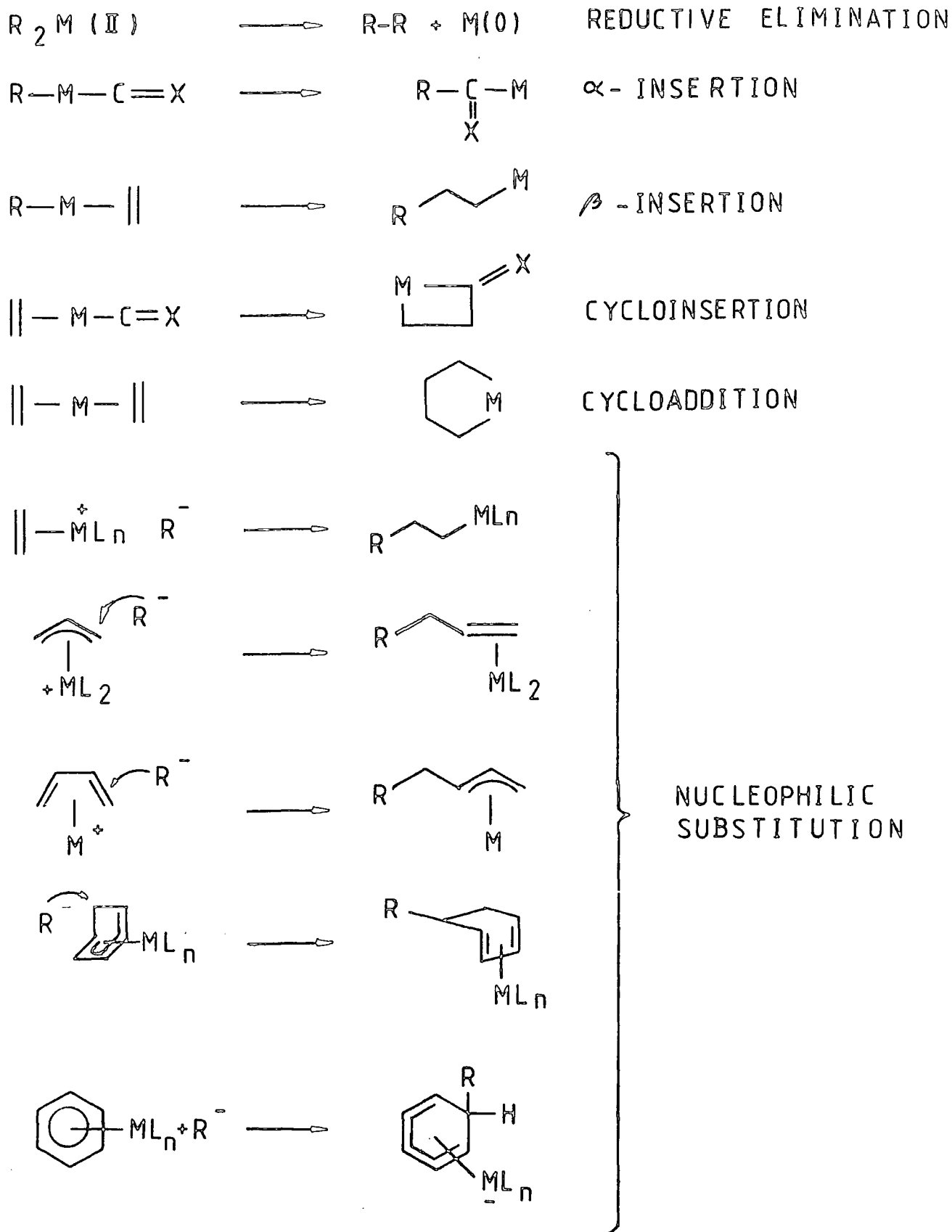
SCHEME 2

1.2. HYDROCYANATION OF ALKENES

Without some form of catalysis, HCN will not react with most carbon-carbon double or triple bonds. Hydrogen cyanide adds to the electron-rich alkene, 1,1-bis(dimethylamino)-ethylene, without additional catalyst, presumably via initial proton transfer to give an intermediate carbocation.

The simplest form of catalysis involves the use of a base. However, base-catalysed addition of HCN only occurs with electron poor olefins which are activated towards nucleophilic attack, e.g. polyhaloalkenes and conjugated systems such as 1:

$$R\!\!\diagdown\!\!C\!\!=\!\!C\!\!\diagup\!\!X$$
$$R\!\!\diagup\qquad\diagdown\!\!R$$

1

$$X = COOR, CN, COR, CHO, Ar$$
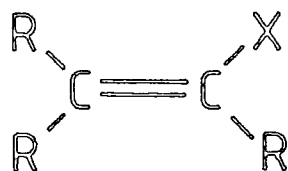
Suitable bases include alkali metal cyanides, hydroxides and carbonates and also pyridine and triethylamine. This form of catalysis is dependent upon the generation of cyanide ions.

Organometallic complexes also catalyse the addition of HCN to both activated and unactivated olefins. Most reports on the topic, particularly before 1980 appear in the patent literature. Of those complexes which catalyse the addition of HCN to activated olefins, the most effective appears to be $Ni(CN)_4^{4-}$ [2]. Although $Ni[P(OR)_3]_4|P(OR)_3$, [3] and $Pd[P(OR)_3]_4$ [4] are also effective, there are no apparent advantages of metal

catalysts over basic catalysis for hydrocyanation of activated olefins.

1.2.1. Hydrocyanation of Less Activated and Unactivated Olefins

Olefins which are not activated by conjugation with a system involving a heteroatom exhibit differing reactivities due to various effects, for example:-

(i)   increased reactivity due to conjugation with another double bond as in a conjugated diene;

(ii)   increased reactivity due to strain, e.g. the double bond in norbornene;

(iii)   decreased reactivity of an isolated double bond, relative to that of ethene, owing to the electron releasing properties and steric bulk of alkyl groups compared to hydrogens.

1.2.2. Butadiene Hydrocyanation

The most intensively studied olefin hydrocyanation reaction is the addition to butadiene. The 1:1 addition of HCN to butadiene to give pentene nitriles catalysed by $Ni(CO)_4$ was the first reported use of transition metal complexes as homogeneous hydrocyanation catalysts [5].

The interest in butadiene hydrocyanation centres on the use of adiponitrile as a precursor in the production of nylon 66, which has been made by DuPont since the 1930's. The development of their homogeneous nickel complex catalysed adiponitrile process is an outstanding example of the successful development of an organotransition metal catalyst for an industrial process. Prior to the opening of the first plant using the above process in 1971, adiponitrile was made by electrolysis of sodium

chloride to give chlorine and sodium hydroxide. Sodium cyanide was made by reacting HCN with the hydroxide, then chlorine was allowed to react with butadiene; after displacement of the chlorine with cyanide, the 1,4-dicyanobut-2-ene formed was hydrogenated to give adiponitrile [6]. The electrolysis and handling of chlorine made the direct addition of HCN to butadiene extremely desirable.

Many other complexes catalyse the 1:1 addition of HCN to butadiene including $Co_2(CO)_8$ [7]; $CoH[P(OPh)_3]_4$ [8], $Ni[P(OR)_3]_4$ [4,9], $Pd[P(OR)_3]_4$ [4] and CuCl [10]. In most of these systems a mixture of nitrile products is obtained, with the 1,4 addition product predominating.

Once hydrocyanated, the unsaturated mononitriles are much less reactive to further hydrocyanation. The 1,4 addition product, pent-3-ene nitrile cannot give adiponitrile by further direct hydrocyanation. In all the above-mentioned catalyst systems, only zerovalent nickel and palladium phosphite complexes, in the presence of Lewis acid promoters catalyse the addition of a second mole of HCN. Adiponitrile is formed in a stepwise process involving catalysis of double bond isomerization to give 4-pentenenitrile, followed by anti-Markovnikov addition of HCN.

The use of Lewis acids to considerably extend catalyst lifetimes and to promote catalytic activity in certain systems. (as well as modify stereoselectivity), was discovered by accident [11]. Sodium borohydride had been added to reactions in an attempt to inhibit the irreversible oxidation of the zerovalent metal by excess HCN. The borohydride did not reduce

the metal back to the zerovalent state however. Instead, it was found that trialkylboron compounds were being produced by reaction of HCN, $NaBH_4$ and 3-pentene nitrile.

A variety of Lewis acids are now known to be useful as promoters and the most widely used are $ZnCl_2$, $AlCl_3$, and trialkyl or triarylboranes.

Before considering other olefins which can be hydrocyanated, it is appropriate at this stage to exemplify the conditions used in typical hydrocyanation reactions.

(a)   Metal Complex. The most successful and widely used metal complexes are zerovalent phosphite or phosphine complexes. Nickel is a fairly expensive metal to use industrially, but the high turnover of these catalysts offsets this disadvantage. Zerovalent palladium complexes are as efficient and versatile as nickel equivalents. For some specific applications (see below) they are more effective. The disadvantage of palladium, and the reason for the relatively small number of investigations into the utility of palladium complexes, is the very high cost of palladium itself.

Cobalt catalysts are both expensive and less efficient, requiring low substrate to catalyst ratios (of about 9:1). Iron systems are poorer than cobalt.

Copper(I) systems have the advantage of lower cost and are still under investigation [10,12,13]. However, copper(I) complexes will only catalyse the monoaddition of HCN to butadiene. Molybdenum, tungsten, ruthenium and rhodium catalysts have been used, but are equally expensive and offer little or no advantage over nickel or palladium.

(b) <u>Temperature and pressure</u>. With nickel catalysts, temperatures in the range -25°C to 200°C and pressures from 0.05 to 100 atmospheres have been used. The exact temperature required for reaction varies with the nature of the catalyst and substrate, but is generally between room temperature and 150°C. The pressure used is normally between 1 and 10 atmospheres.

(c) <u>HCN</u>. Catalyst poisoning occurs by irreversible oxidation of the nickel species present to a nickel(II) dicyanide complex which precipitates from solution. Thus it is necessary to avoid the use of an excess of HCN. In a continuous flow process involving controlled addition of HCN to the reaction mixture at the rate at which it is consumed, the problems of catalyst deactivation are minimised.

(d) <u>Excess ligand</u>. Addition of free ligand suppresses the formation of the dicyanide mentioned above, but slows down the hydrocyanation reaction, therefore the amount of excess ligand added must be chosen carefully. The ligand to metal ratio used varies from two to twenty.

(e) <u>Solvent</u>. Many alkenes are liquids and can act as solvents for the reactions themselves. Solid, gaseous or expensive alkenes can be hydrocyanated in a wide variety of solvents. The aromatic hydrocarbons, toluene or benzene are convenient. It has been reported that some solvents such as ethers [3b] (e.g. dioxan, trioxan, THF) or phenolic solvents [14,15] improve yields and alter product distributions.

(f) The addition of Lewis acids, in concentrations equal to, or slightly greater than, that of the metal catalyst can have pronounced effects on the catalyst life and stereoselectivity of

hydrocyanation reactions. The observed effects vary greatly, depending on the catalyst, substrate and type of Lewis acid. For example, the rate of hydrocyanation of propylene is much faster in the presence of $AlCl_3$, yet is unaffected by $ZnCl_2$ and is slowed down by BPh_3 [11]. Both $AlCl_3$ and $ZnCl_2$ accelerate the hydrocyanation of 1-hexene [15].

The change in the stereoselectivity of reactions is again not easily rationalised [15]. Lewis acids increase the amount of linear nitrile obtained in the nickel catalysed hydrocyanation of 1-hexene. An increase in the amount of linear nitrile was also observed in the nickel catalysed hydrocyanation of styrene when triphenylboron was added to the reaction. However, the use of $AlCl_3$, $ZnCl_2$, $B(OPh)_3$, BCy_3 and $B(o-tolyl)_3$ did not alter product distribution [16].

1.2.3. Other Dienes

Hydrocyanation catalysed by nickel(0) complexes is a general reaction for hydrocarbon dienes [11]. Both conjugated and non-conjugated dienes undergo hydrocyanation to give mono, and in many cases, dinitrile products. Unconjugated dienes often give products resulting from addition to isomerized olefin. $Co_2(CO)_8$ and CuCl also catalyse the hydrocyanation of dienes.

1.2.4. Monoolefins

(a) Simple alkenes. Addition of HCN to terminal alkenes is catalysed by Ni(0), Co(0) and Pd(0) complexes. In general, the yields of nitrile obtained decrease as the alkene chain length increases. The product can be either a linear or branched nitrile. The ratio of linear to branched isomers is sensitive

to the catalyst type, the nature of the substrate and the presence of Lewis acids. Steric hindrance in the substrate is the most important factor in determining the ratio. When propylene is hydrocyanated using NiL_4 (L = tri-p-tolyl phosphite) and $AlCl_3$ promoter, the linear to branched ratio is 1.5. Under the same conditions 1-hexene gives a ratio of 19 whereas with 3,3-dimethylbutene, 2,3-dimethyl-1-butene and isobutene, no branched product is detected [15,17]. Hydrocyanation of styrene gives 91% branched nitrile. This change in selectivity is most probably due to preferential stabilization of the branched over the linear intermediate during the catalytic cycle. This may be ascribed to a stabilising interaction between the aromatic ring and the metal. The effect of Lewis acid on the selectivity has been discussed above.

The preference towards branched nitrile in the hydrocyanation of styrene has been utilized recently in developing a new route to the anti-inflammatory drugs ibuprofen 2 and naxproxen 3. These compounds are readily prepared by the
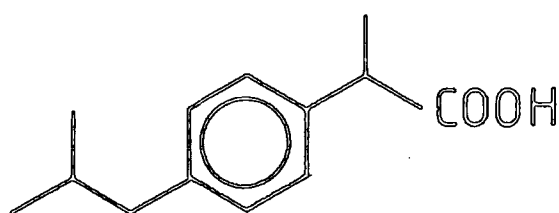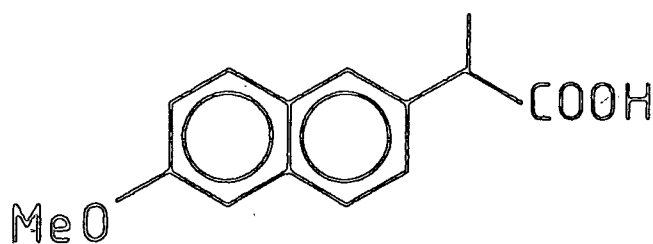
2   3

Markovnikov addition of HCN to the appropriate vinyl arenes (which are relatively easy to prepare). These reactions are catalysed by $Ni(P(p-tolyl)_3)_4$ in toluene [18], (Scheme 3).
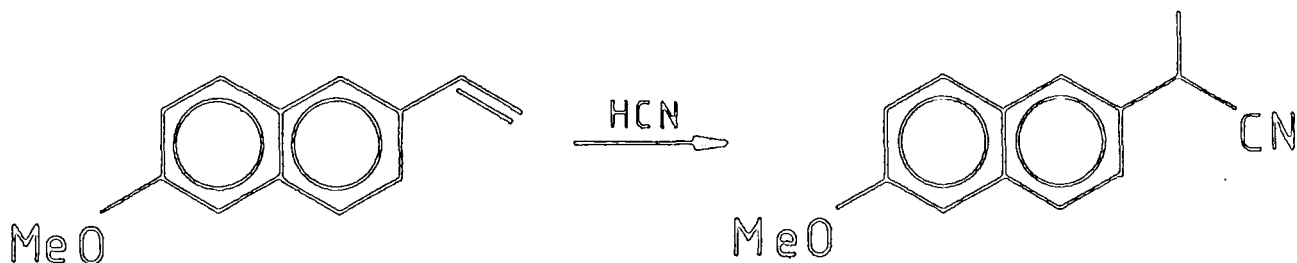
Scheme 3

The nitrile may be easily hydrolysed to give **3**. A similar procedure is applicable to the preparation of **2**.

Internal double bonds are less reactive than terminal ones. However, the nickel complexes present in the reaction also act as highly efficient double bond isomerization catalysts, particularly in the presence of Lewis acids [11,15]. The products of isomerization processes are formed under kinetic control. It is well established therefore, for isomerization to occur to give thermodynamically less stable alkenes which may undergo subsequent hydrocyanation.

(b) <u>Cyanoolefins</u>. The reaction of these olefins is of particular relevance to the adiponitrile process. Cyanoolefins in which the CN group is separated from the olefinic carbon by at least one C atom e.g. 3- or 4-pentenenitrile are readily hydrocyanated at 25°C using a nickel phosphite catalyst system. Other catalysts are unable to effect this addition. Some conjugated cyanoolefins are not hydrocyanated without the addition of a Lewis acid. The changes in product distribution caused by addition of various Lewis acids are similar to those of styrene, triphenylboron greatly slows the reaction and increases product linearity to almost 100%. Other triarylborons

can either improve, not affect, or worsen product linearity.

(c) <u>Monoolefins which are difficult to hydrocyanate</u>. Virtually nothing has appeared in the literature concerning olefins which cannot be hydrocyanated using metal catalyst systems. Tolman and co-workers have published a list of olefins which the Nickel[P(O-o-tolyl)$_3$]$_3$ catalyst cannot hydrocyanate [11]. These are all olefins containing heteroatoms and most are conjugated to strongly electron withdrawing groups e.g. tetracyanoethene (TCNE), C_2F_4 etc.

Electron-deficient alkenes e.g. C_2F_4, fumaronitrile and maleic anhydride fail to react because they poison the catalyst system. Conjugated cyanoolefins precipitate insoluble nickel complexes from reaction mixtures, although this may be prevented by the presence of Lewis acids. Possible explanations of these important effects are discussed in the section dealing with the mechanism of hydrocyanation.

(d) <u>Strained olefins</u>. The addition of HCN to double bonds which are activated due to strain has been studied for nickel and palladium triarylphosphite complex catalysts. Norbornadiene gives various dicyanides. Norbornene is hydrocyanated to give exclusively the exo product, <u>5</u> in the presence of palladium complexes [19,20,21]. This pronounced stereoselectivity in HCN addition is likely to be due to preferred binding of the alkene to the metal by the less hindered face. Cobalt octacarbonyl also catalyses HCN addition to norbornene but gives a mixture of exo and endo products.
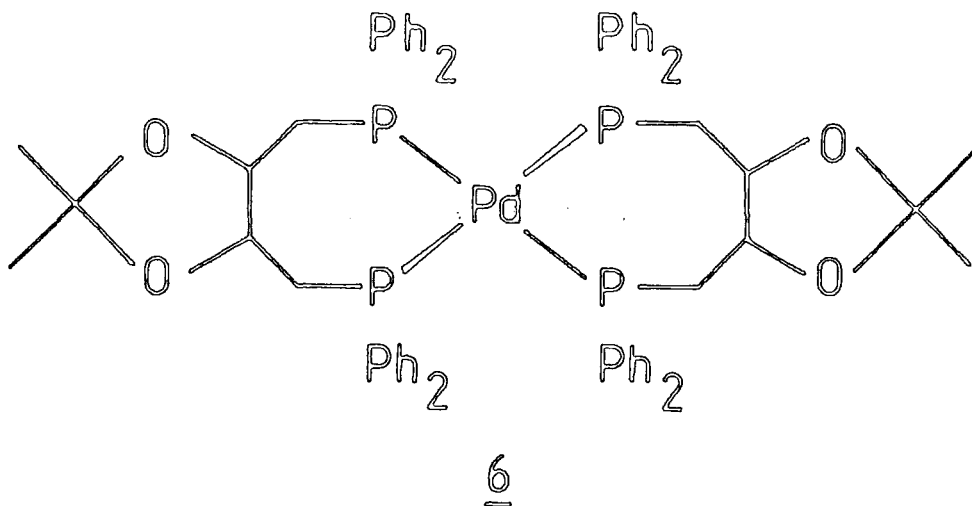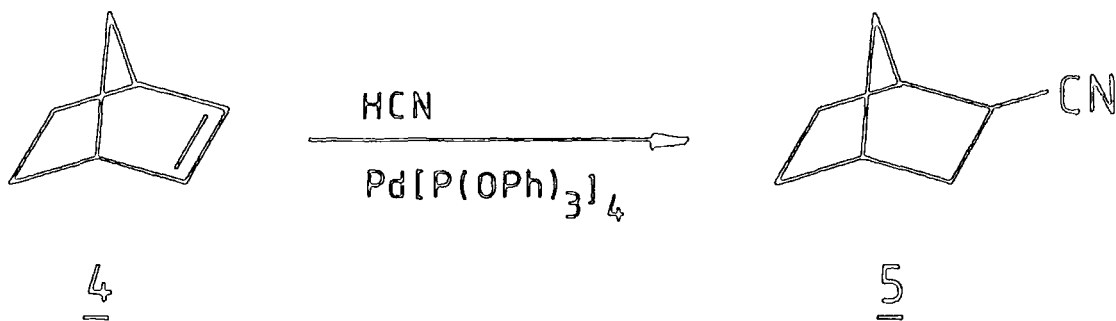
1.3. ASYMMETRIC HYDROCYANATION

The only reported catalyst for the asymmetric addition of HCN to a substrate is bis DIOP Palladium(O) 6 [20,21]. This system has been studied in detail by W.R. Jackson and co-workers. The products of the hydrocyanation of norbornene and related olefins are enantiomerically enriched. The product norbornane carbonitrile, 5 obtained in a typical hydrocyanation of norbornene was claimed to be 31% enantiomerically pure. However studies described in this thesis will reveal that this figure is incorrect. The enantiomer excess is nearer 13%. The nickel analogue of the palladium DIOP$_2$ complex did catalyse the reaction, but both preparative and optical yields were considerably lower. The analogous platinum complex, Pt(DIOP)$_2$ was catalytically inactive.

Other chelating ligands tested for the palladium catalysed asymmetric hydrocyanation were diphin 7. 3α and 3β-diphenylphosphino-2α-(2'-diphenylphosphinoethyl)-5α-cholestanes 8a and b.
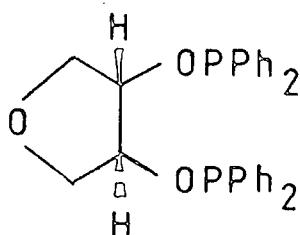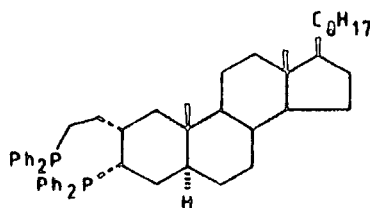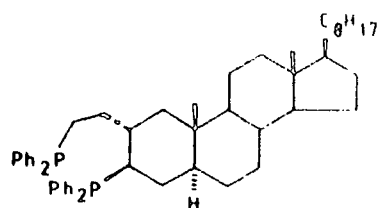
7   8a   8b

Once again, both preparative and optical yields were very low [22].

1.4. MECHANISM OF HYDROCYANATION

In order to improve or develop the use of any reaction, an understanding of the mechanism is vital. The mechanism of homogeneous transition metal catalysed hydrocyanation was not well understood at the start of this Ph.D. project. Most of the work relating to mechanistic studies has been published since 1984.

Many separate pieces of information are required in order to build up an accurate picture of a mechanism. These include:

(i)   stereochemistry of the product;

(ii)   detection or isolation of intermediates;

(iii) detection of any rearrangement or exchanges in the

product and/or starting materials;

(iv)   the form of the rate law, i.e. a kinetic analysis;

(v)   the effects of solvent polarity and radical
         scavengers.

The best studied reaction is the nickel phosphite catalysed
addition of HCN to alkenes. In particular ethene hydrocyanation
has been studied by Tolman and co-workers. In this case a clear
picture of the mechanism is emerging. Preliminary studies for
this work on relevant equilibria in nickel(0) complexes were
initiated by DuPont workers in the early 1970s (see later).

The mechanism appears to be related to that of
hydroformylation reactions, which are much better studied. The
similarities include

(i)   initial loss of a ligand from a coordinatively
         saturated low valent metal complex;

(ii)   oxidative addition to the complex to give a metal
         hydride species;

(iii)   subsequent olefin bonding followed by insertion to
         give a metal alkyl;

(iv)   a carbon-carbon bond forming step which involves
         migratory insertion to coordinated CO or CN,
         indicated by the fact that in both cases addition is
         cis stereospecific;

(v)   product formation by reductive elimination.

Although all hydrocyanations catalysed by zerovalent metal
complexes probably involve the same steps, the mechanism will
vary with the nature of the solvent, ligand, alkene and the
metal catalyst.

A typical reaction scheme proposed for alkene hydrocyanation is given in <u>Scheme 4</u>.

[M] (0)   + HCN $\xrightarrow{\text{(ii)}}$ H-M(II)
                                                              |
Coordinatively   CN
unsaturated complex

RCN   C=C | (iii)
        (iv,v)   ↓

R   C=C
| |
M(II)   ←(iii)   H-M(II)
| |
CN   CN
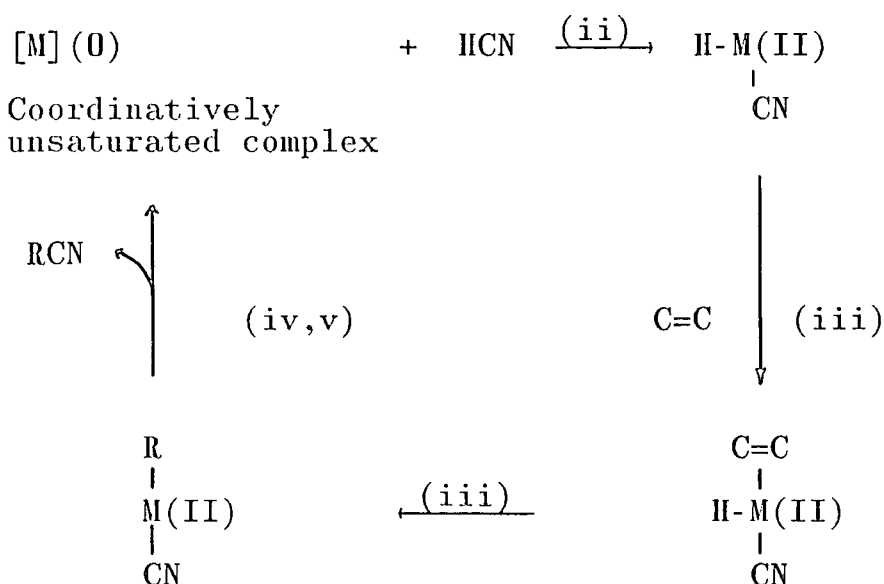
<u>Scheme 4</u>

The most important physical technique which has been used to examine the mechanism is N.M.R. Spectroscopy. In particular ^{1}H and [31]P N.M.R. have been used to obtain information on the structure of intermediates and rates of exchange of phosphorus ligands, observe product formation, and determine the structure of the products from isotopic labelling experiments. Optical spectra have been used to examine the equilibria of some relevant complexes. Infra-red spectra have also found some use. The position of the distinctive $-C\equiv N$ stretch around 2100 - 2300 cm^{-1} indicates different types of coordinated cyanide. Such

studies parallel the use of infra-red spectra in the examination of metal carbonyl chemistry.

The metal complexes which are actually added to the reaction mixture are pre-catalysts. The fact that the addition of free ligand, which suppresses catalyst deactivation, also slows down the overall rate of hydrocyanation, indicates that ligand dissociation is a likely first step in the production of the active catalyst. Tolman has studied ligand dissociation and exchange reactions for zerovalent nickel complexes, in solution. Steric and electronic effects were examined. The steric effects were probed by determining ligand cone angles from molecular models, and electronic effects by measuring $\nu_{C=O}$ in $Ni(CO)_3L$ complexes. The most important result to follow from these studies is that steric, rather than electronic effects dominate the reactivity of nickel(0) phosphine and phosphite complexes [23-28]. For example, the ability of phosphorus ligands to displace one another from zerovalent nickel complexes depends on the steric bulk, i.e. the cone angle of the ligand, rather than its electronic properties. The complex of the sterically small $P(OEt)_3$ ligand exists as undissociated $Ni[P(OEt)_3]_4$, even when warmed above room temperature, whereas the complex with the bulky PPh_3 ligand is totally dissociated in solution, to give free PPh_3 and $Ni(PPh_3)_3$, even at low temperatures.

In the solid state the complexes mentioned above exist as NiL_4. The isolation of solid NiL_3 complexes has allowed a detailed study of the role of these 16 electron intermediates [29].

The position of the equilibrium in <u>Scheme 5</u> depends on the

$$RCN + NiL_4 \rightleftharpoons RCNNiL_3 + L$$

Scheme 5

nature of L. The greater the steric bulk of the ligand, the further to the right the equilibrium lies. When examining the reaction of olefins with the nickel complexes, it was found that the position of the equilibrium (Scheme 6), varied according to the steric and electronic properties of the particular olefin

$$Olefin + NiL_3 \rightleftharpoons (Olefin)NiL_2 + L$$
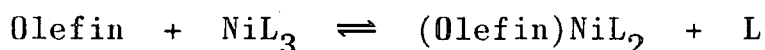
Scheme 6

and ligand involved [30-35].

In the case of cyanoolefins, the relative amounts of olefin bound and cyano bonded complexes depended on the amount of added free ligand. The greater the concentration of added free ligand, the more nitrile bonded complex is present. This may be related to the different stoichiometries involved.

1.4.1. Oxidative Addition

Having considered the dissociation of the nickel complexes, and their interactions with various components of the reaction mixture, the next step to examine in the catalytic cycle is oxidative addition. In general, oxidative addition can occur

either by an ionic or a radical mechanism. Coordinatively
unsaturated complexes are more reactive towards oxidative
addition. The most common type of addition involves an overall
two electron change, increasing the formal oxidation state of
the central metal by 2. In the case of zerovalent nickel.
palladium and platinum, this results in a change from a d^{10}
configuration with a maximum coordination number of four to a d^8
configuration with a maximum coordination number of five for an
eighteen electron complex.

An example of a simple oxidative addition is the reaction
of low valent metal complexes with protonic acids to give
transition metal hydrides. Hydride complexes are common in
transition metal complex chemistry, and are known for the whole
transition metal series. They are known to be intermediates in
many catalytic and stoichiometric reactions of transition metal
complexes. If the hydride formed is unsaturated, and positively
charged, then the conjugate base will usually add giving a
neutral complex. Sometimes nucleophilic attack of the conjugate
base, e.g. the chloride ion may precede hydride formation. In
non-polar solvents, additions may be concerted.

Studies of the oxidative addition of hydride to zerovalent
nickel, palladium and platinum complexes have been carried out
using both HCN and strong inorganic acids. Most studies were
concerned with nickel complexes, and were carried out in the
1960s.

Cariati and co-workers examined the reaction of $Pt[P(Ph)_3]_4$
with various acids [36]. They showed that the four coordinate
hydride complexes 9 and 10 were formed, depending on the

solvent and the coordinating power of the anion. HCN addition
gave the trans covalent complex $\underline{9}$. It was also reported that

$$PtHX(PPh_3)_2 \qquad\qquad [PtH(PPh_3)_3]^+X^-$$

$$\underline{9} \qquad\qquad\qquad \underline{10}$$
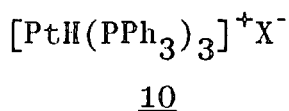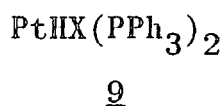
attack of acids on nickel and palladium triphenylphosphine
complexes liberated hydrogen gas and did not give stable metal
hydrides. Drinkard and co-workers [37] reported that the
complexes obtained from the protonation of nickel(0)
triethylphosphite by strong acids in various organic solvents
were hydrides. They differed from those reported by Cariati in
that they were coordinatively saturated cations with five
ligands, such as $NiH[P(OEt)_3]_4^+$. Stable hydrides formed by
protonation of the nickel(0) complex of the chelating
biphosphine 1,2-bis(diphenylphosphino)ethane were isolated from
toluene solutions by Schunn [38]. ^1H N.M.R. and other
spectroscopic techniques were used to confirm that these
complexes were also five-coordinate hydride cations with a
non-coordinating anion e.g. $\underline{11}$.

$$NiH[Ph_2P(CH_2)_2PPh_2]_2^+AlCl_4^-$$

$$\underline{11}$$
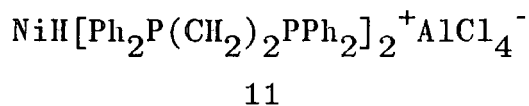
Initial studies by Corain et al. [39] suggested that when HCN was reacted with the Ni(0) complex of 1,4-bis(diphenylphosphino)butane, the product was not a hydride, but a mixture of phosphine bridged Ni(I) and Ni(II) cyanide complexes. However Tolman later showed [40] that the product was actually a Ni(II) hydridocyanide complex <u>12</u>, in which one of the phosphines was monodentate. The hydride signal in the ^{1}H N.M.R. spectrum may not have been observed previously due to intermolecular phosphine exchange, causing broadening of the hydride resonance.

$$
\underset{\underline{12}}{\overset{\overset{\displaystyle \text{H}}{|}}{\underset{\underset{\text{CN}}{|}}{\text{Ni-P}}}}
$$

$\left(\begin{array}{c}P\\P\end{array}\right.$ = 1,4-bis(diphenylphosphino)butane
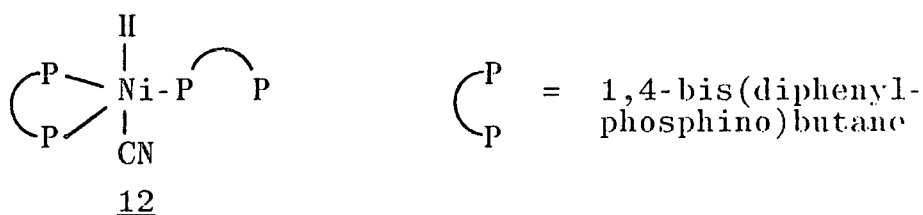
HCN reacts similarly with zerovalent nickel(0) complexes of monodentate phosphines in toluene to give non-ionic five-coordinate nickel(II) complexes which are probably trigonal bipyramidal in structure. This is consistent with the strong coordination of the cyanide ion, and may also be related to the non-polar nature of the solvent and the fact that HCN is a weak acid. In other solvents and/or in the presence of Lewis acids, ionic structures may be important for cyanide complexes. The cationic hydrides are powerful olefin isomerization catalysts whereas the phosphine complexes are not [41]. The mechanism of isomerization involves ligand dissociation from $HNiL_4^+$.
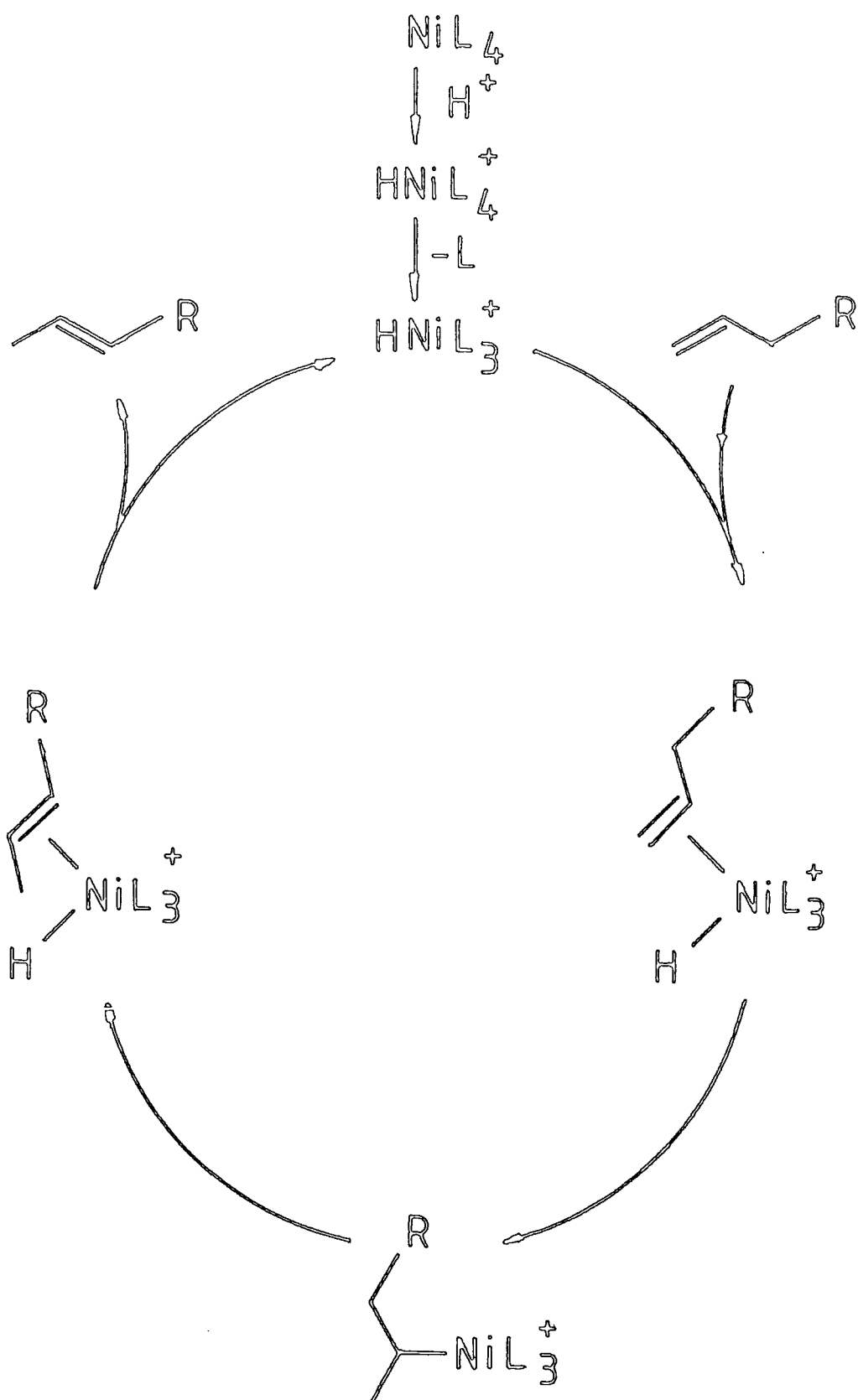
SCHEME 7

Protonation of NiL_4 complexes greatly labilizes the ligands [42] although ligand dissociation is still the rate limiting step in the olefin isomerization reaction mechanism. Olefin coordination, insertion into the NiH bond, followed by β hydrogen abstraction, then product dissociation to regenerate $HNiL_3^+$; complete the catalytic cycle for olefin isomerization. Scheme 7.

Structures and stability of the neutral $HNiL_nCN$ complexes depend on both the electronic and steric properties of the phosphorus ligand. The reaction between NiL_4 complexes and HCN requires ligand dissociation as an initial step. Thus, in toluene, the rate of reaction of HCN with NiL_4 complexes depend on the rate of ligand dissociation from NiL_4. Electron withdrawing ligands decrease the basicity of the nickel atom, decreasing the equilibrium constant for dissociation of NiL_4. Complexes of bulky ligands react faster with HCN as dissociation is easier. If a sufficiently bulky ligand is used the $HNiL_3CN$ may lose a further ligand to form the 16 electron $HNiL_2CN$ complex. Lewis acids, particularly triarylboranes have been shown to coordinate to the nitrogen lone pair of the cyano-group in nickel hydridocyanide complexes [16]. The stability of these complexes can therefore be altered by Lewis acid coordination (Scheme 8).

$$HNiL_3CN \quad + \quad BPh_3 \quad \rightleftharpoons \quad HNiL_3CN.BPh_3$$
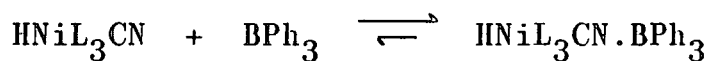
Scheme 8

1.4.2. <u>Olefin Binding</u>

Tolman has studied the interaction between olefins and zerovalent nickel complexes, and has briefly examined palladium and platinum analogues [30-33,43].

The complex $(C_2H_4)Ni[P(O-o-tolyl)_3]_2$ was prepared and isolated by triethylaluminium reduction of nickel acetylacetonate in the presence of two equivalents of ligand and excess ethene. The complex was found to be stable to dissociation but very labile in exchange with both added ligand and free ethene. The same complex was formed by addition of ethene to a solution of NiL_3 or NiL_4. The reactions of 38 olefins with $Ni[P(O-o-tolyl)_3]_3$ were observed and it was found that electron withdrawing substituents gave more stable olefin complexes, with substituent resonance effects being more important than inductive effects. Alkoxy and acetoxy substituents destabilise the complexes. The order of complex stability for simple olefins is ethene > styrene > propene > 1-hexene > disubstituted alkenes.

[1]H N.M.R. studies of the reaction of ethene with $Pd[P(C_7H_7)_3]_3$ complexes showed [43] that addition of ethene to deuterobenzene solutions of the complexes gave a sharp ethene resonance slightly to lower frequency than that of free ethene ($\Delta\delta$ 0.25 ppm), which returned to the position of free ethene on adding one equivalent of phosphine ligand. Exposure of a solution of palladium tetrakis(triphenylphosphine) to ethene gave a sharp resonance due only to free ethene. In the case of nickel and platinum complexes $(C_2H_4)M[PPh_3]_2$ the resonance due to bound ethene occurred to lower frequency than that of free

ethene ($\Delta\delta$ 2.65 ppm). The bound ethene resonance remained sharp and moved to higher frequency as more ethene was added to a solution of $(C_2H_4)Ni[PPh_3]_2$, whereas with the platinum analogue, a broad new resonance appeared at the position of free ethene. This information suggests rapid olefin exchange in the nickel and palladium complexes, and slower exchange in the platinum complex. The small shift in the ethene signal for the palladium system indicates a very low complex formation constant. Combination of the [1]H N.M.R. data with information from optical spectra allowed the calculation of equilibrium constants for the reaction

$$ML_3 \; + \; C_2H_4 \; \rightleftharpoons \; (C_2H_4)ML_2 \; + \; L$$
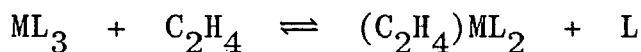
These were found to be 300, 0.12 and 0.013 for M = Ni, Pt and Pd ($L = P(C_6H_5)_3$) [43].

1.4.3. <u>Alkyl Formation</u>

The hydrocyanation of ethene catalysed by nickel(0) P(0-o-tolyl)$_3$ has been extensively studied [16,44,45] because the system gives relatively high concentrations of many of the catalytic intermediates. The complex used as the starting point for these studies, which is presumed to be a key intermediate in the catalytic cycle, was $(C_2H_4)Ni[P(0-o-tolyl)_3]_2$. In the presence of excess ethene, addition of HCN at -40°C to $(C_2H_4)Ni[P(0-o-tolyl)_3]_2$ gives three isomeric complexes [13a-c].

The same intermediates may be generated by addition of excess ethene to $HNi[P(0-o-tolyl)_3]_3CN$ at -50°C. They each have different [31]P N.M.R. chemical shifts. It is not known whether

$$CH_2=CH_2$$
$$L-Ni-C_2H_5$$
$$CN$$

13(a)

$$L$$
$$CH_2$$
$$\parallel{}^2-Ni-C_2H_5$$
$$CH_2$$
$$CN$$

(b)

$$CH_2=CH_2$$
$$NC-Ni-C_2H_5$$
$$L$$

(c)
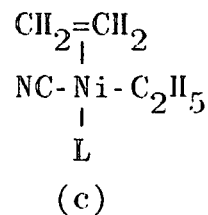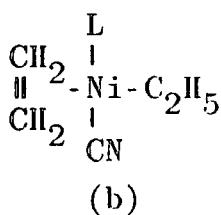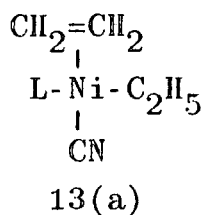
all the isomers take part in the catalytic cycle, and the rate of interconversion between isomers appears to be faster than the rate of hydrocyanation.

The formation of alkyl cyanide complexes 13a-c conflicts with earlier work by Tolman [26] in which the production of an alkyl with the structure $EtNiL_2CN$ was suggested following addition of HCN to $(C_2H_4)NiL_2$. The difference in ^{31}P chemical shifts between the isomers is quite small ($\Delta\delta \sim 0.5$ ppm), and the signals are exchange broadened except at low temperatures. Tolman and co-workers believe that with olefins which bond less strongly than ethene or with better coordinating phosphorus ligands, the bound olefin in intermediates such as 12 is replaced by a phosphorus ligand. In some mechanistic schemes they accordingly use the symbol L to denote either olefin or phosphorus ligand.

Other olefins produce much less stable alkyls, most of the nickel remaining as $HNiL_3CN$ in solutions containing the hydridocyanide and olefin. The fact that ethene forms the alkyl complexes much more readily than other olefins [16] may explain why the rate of ethene hydrocyanation is much faster than that of other alkenes.

Steric factors in the alkyl intermediates appear to dictate
product distribution. Tert-butyl ethene and propene give mostly
linear product due to steric crowding in the branched
intermediate (see below). The preference for branched product
in the case of styrene is accounted for by the stabilization of
the branched alkylnickel cyanide complex by interaction of the
aromatic ring with the metal centre, 14.

14
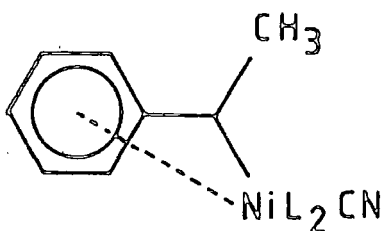
The hydrocyanation of dienes has been extensively studied
by Tolman et al. In these cases, the addition of the first mole
of HCN proceeds via π-allyl intermediates. The addition of the
second mole of HCN proceeds via σ-alkyl intermediates analogous
to the alkyls formed in the reactions of monoolefins. The
π-allyl intermediates are much more stable than the σ-alkyl
intermediates. Reaction mixtures of 0.5M butadiene, 0.5M
Ni[P(OEt)$_3$]$_4$ and 0.6M HCN in CH$_2$Cl$_2$ or CD$_2$Cl$_2$ were examined by
^{1}H and ^{31}P N.M.R., optical and infra-red spectroscopy [46]. A
stable syn-1-methyl π-allyl nickel cyanide complex 15 was
detected, decay of which was suggested to be the rate
determining step in the hydrocyanation.

The fact that allyl chloride cannot be hydrocyanated with
nickel(0) catalysts has been explained by the oxidative addition
of the chloride to give a stable nickel II π-allyl chloride

$$\text{---NiL}_2\text{CN}$$

15
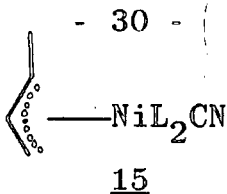
complex [11]. Lewis acids have been shown to catalyse the oxidative addition of allyl cyanide to nickel(0) complexes to give nickel II π-allyl cyanides.

1.4.4. Reductive Elimination and the Catalytic Cycle

McKinney and Roe have investigated the same nickel(0) catalysed hydrocyanation as Tolman and co-workers, with particular emphasis on the product forming reductive elimination step [44]. They have found that in the case of ethene hydrocyanation, propanenitrile is produced by reductive elimination which occurs by an associative process. Associative reductive elimination is relatively rare; in this process the rate of elimination is accelerated by added ligand. Most reductive eliminations occur by "direct reductive elimination" where the rate of elimination is independent of added ligands, or by "dissociative reductive elimination" which requires ligand dissociation to give a three coordinate intermediate.

In the case of ethene hydrocyanation magnetization transfer experiments looking at ^{31}P N.M.R. resonances, as well as kinetic studies [44-45], have shown that reductive elimination occurs from an unobservable five coordinate nickel II complex **16**.

$$\begin{array}{c} \text{L} \quad \overset{\displaystyle \text{L}}{\underset{|}{}} \quad \text{C}_2\text{H}_4 \\ \diagdown \overset{|}{\underset{\diagup \diagdown}{\text{Ni}}} \diagup \\ \text{NC} \qquad\quad \text{Et} \end{array}$$

16
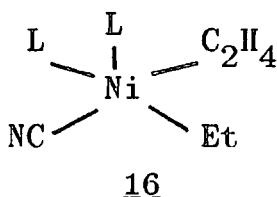
Combining the information from the complexes and reaction steps studied, McKinney and Roe have proposed a mechanism for the hydrocyanation of ethene by $Ni(C_2H_4)[P(O-o-tolyl)_3]_2$ [44]. Their scheme differs from those published earlier [16], and also includes a consideration of non-productive equilibria in a separate cycle. The proposed mechanism, (Scheme 9) begins with the rapid oxidative addition of HCN to the 16 electron complex 17 to give the adduct 18 which dissociates a ligand to give the hydride 19. Addition of ethene combined with insertion of coordinated ethene into the Ni-H bond generates the isomeric alkyl complexes 13a-c which constitute the only observable nickel species of the catalytic cycle whilst the reaction is proceeding (i.e. in the presence of excess HCN and ethene). The kinetics observed require that the product forming step proceeds by an associative reductive elimination involving the unobserved five coordinate intermediate 16. Reductive elimination from 16 regenerates 17 to continue the cycle and form the product nitrile. 17 is of course stable in the absence of HCN.

A theoretical study [47] suggests that reductive elimination from a dialkyl nickel complex would be more favourable from a five coordinate rather than a four coordinate complex. Elimination from a four coordinate complex would generate a high energy 14 electron NiL_2 species, whereas the product from a five coordinate intermediate is, in this case an isolable 16 electron olefin NiL_2 complex.

1.4.5. Catalyst Deactivation

The nickel catalysts have lifetimes of the order of thousands of cycles of catalyst turnover. Excess HCN

Structure 17 (top)

$$L \diagdown_{\diagup} Ni - \| \begin{array}{c} CH_2 \\ CH_2 \end{array}$$

$$\underline{17}$$

EtCN

HCN

Structure 16 (left)

$$\begin{array}{c} L \\ | \\ L - Ni - C_2H_4 \\ NC \diagup \quad Et \end{array}$$

$$\underline{16}$$

Structure 18 (right)

$$\begin{array}{c} CH_2 = CH_2 \\ | \\ L_2 - Ni - H \\ | \\ CN \end{array}$$

$$\underline{18}$$

L

Structure 13 (lower left)

$$\begin{array}{c} L \\ CH_2 = CH_2 \\ | \\ L - Ni - Et \\ | \\ CN \end{array}$$

$$\underline{13}$$

C_2H_4

Structure 19 (lower right)

$$\begin{array}{c} CH_2 = CH_2 \\ | \\ L - Ni - H \\ | \\ CN \end{array}$$

$$\underline{19}$$
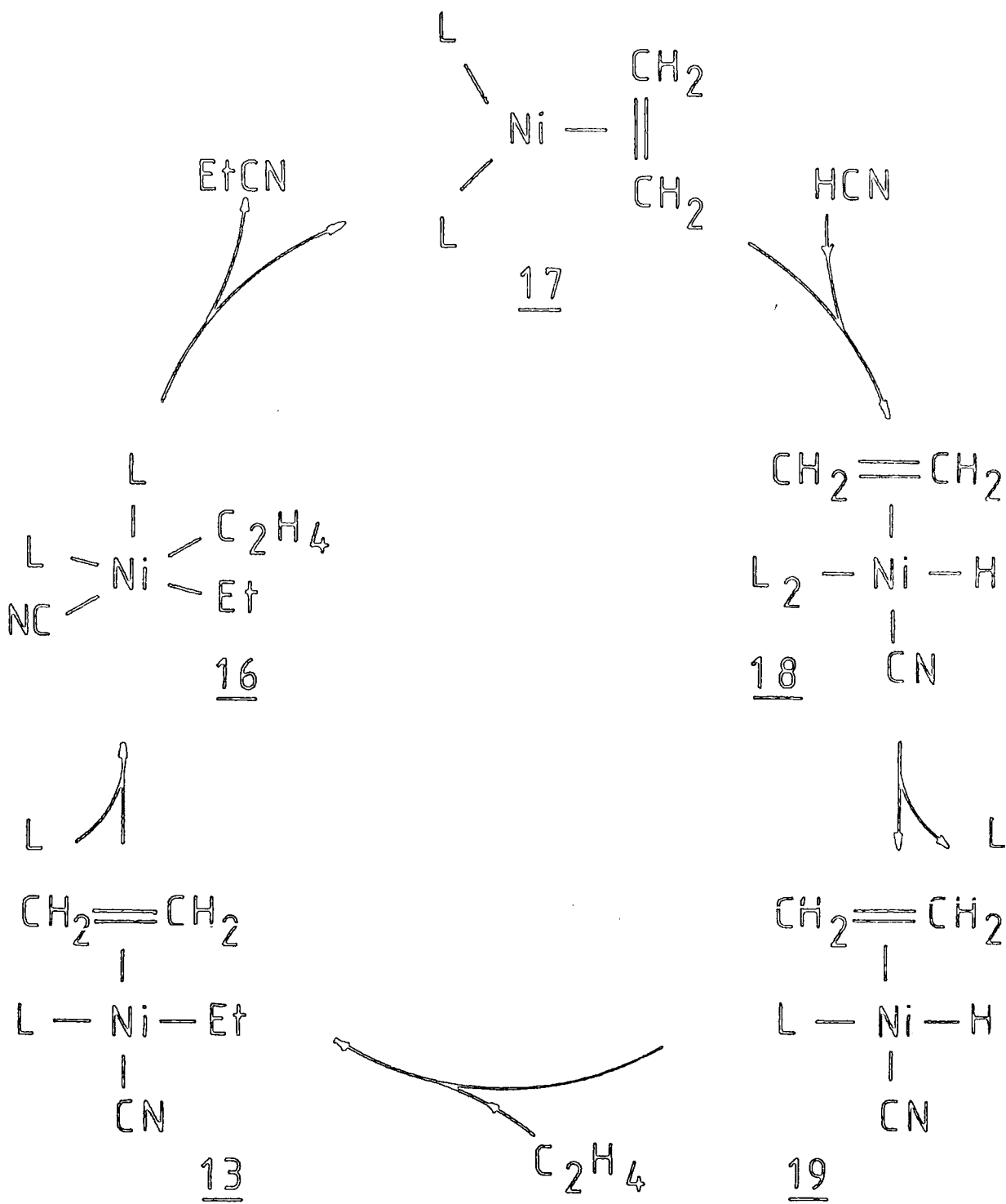
SCHEME 9

considerably reduces catalyst lifetime. Nickel is removed from the system by precipitation as nickel(II) dicyanide. This is formed by irreversible oxidation of complexes within the catalytic cycle, e.g. Scheme 10.

$$R\text{-}NiL_2CN \xrightarrow{\text{HCN}} RNiL_2(CN)_2 \xrightarrow{\text{RH}} NiL_2(CN)_2 \xrightarrow{2L} Ni(CN)_2$$
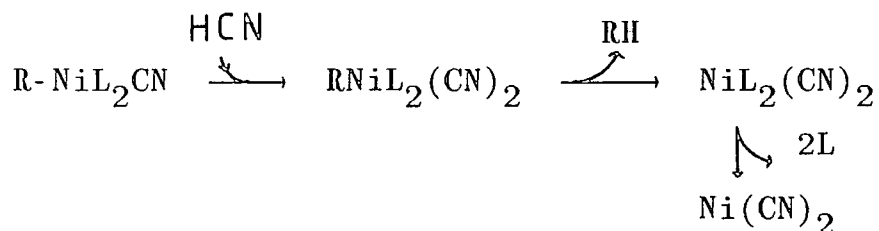
Scheme 10

Added free ligand may suppress this poisoning by reducing the concentration of the coordinatively unsaturated nickel(II) complex

$$NiL_2EtCN \underset{-L}{\overset{+L}{\rightleftharpoons}} NiL_3EtCN$$
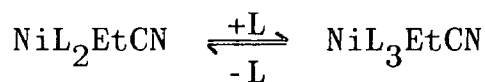
Catalyst deactivation is responsible for the failure of the nickel(0) system to hydrocyanate some olefins [11]. Fumaronitrile and maleic anhydride form stable unreactive (olefin) NiL_2 complexes. Most failures occurred due to electron deficient alkenes forming alkyl nickel cyanide complexes which would not undergo reductive elimination. Conjugated cyanoolefins form α-cyanoalkylnickel complexes which decompose and precipitate as polymers, removing nickel from the system.

1.4.6. The Effects of Lewis Acids on the Mechanism

The ability of Lewis acids to produce dramatic changes in product distribution and reaction rates has been mentioned earlier. The coordination of a Lewis acid to the lone pair of the nitrogen in nitrile groups can disturb equilibria involved in the hydrocyanation reaction. The effects are not clearly understood, being largely empirical. They depend on both the steric and electronic properties of the Lewis acid, the addition of which can improve, worsen or make no change to reaction rates or product distribution.

Druliner has shown [48] that addition of various Lewis acids (denoted A) to $HNiL_3CN$ complexes gave both $HNiL_3CN.A$ and $HNiL_4^+CN.A^-$ species. These were identified by ^1H, ^{13}C and ^{31}P N.M.R. and their I.R. spectra in the $C \equiv N$ stretching region. $H^{13}CN$ was used to confirm assignments. $HNiL_4^+$ species have been shown to be powerful olefin isomerization catalysts, [41].

The extent of Lewis acid coordination varies widely for different Lewis acids. The boranes BPh_3, $B(p\text{-}tolyl)_3$ and $B(CH_2Ph)_3$ have equilibrium constants for coordination $HNiL_3CN$ which are too large to measure directly. The more bulky $B(o\text{-}tolyl)_3$ and $B(Cy)_3$ coordinate relatively little.

Tolman has studied the effects of Lewis acids on some hydrocyanation reactions and on the equilibria involved [16]. The empirical nature of the changes brought about by Lewis acid addition is demonstrated by the finding that the rate of hydrocyanation of 4-pentenenitrile catalysed by NiL_4 complexes is slowed down by addition of BPh_3 for $L = P(O\text{-}o\text{-}tolyl)_3$ but accelerated by BPh_3 addition for $L = P(O\text{-}p\text{-}tolyl)_3$.

Lewis acids can coordinate to any nitrile groups present in the reaction mixture, but spectroscopic studies [16] have shown that adducts with cyanide groups attached to nickel are strongly preferred to coordination of the Lewis acid to free nitriles.

BPh_3 improves the product linearity in the hydrocyanation of 4-pentenenitrile and styrene [16]. The improvement is from 9% to 33% linear product in the styrene reaction, and from 78% to 98% linear product in the reaction of 4-pentenenitrile. $B(p-tolyl)_3$ gives similar but smaller improvements. Other Lewis acids e.g. $B(o-tolyl)_3$, BCy_3, $B(OPh)_3$ do not change product distribution. It has been suggested that BPh_3 coordination to the cyanide group of the alkylnickel cyanide intermediate increases steric crowding around the nickel centre, destabilizing the branched alkyl intermediate over the linear one. Bulkier Lewis acids do not coordinate well enough to affect product distribution.

The strong coordination of BPh_3 to $HNiL_3CN$ complexes is responsible for the acceleration of the reaction rate of the $Ni[P(O-p-tolyl)_3]_4$ catalysed hydrocyanations. Without BPh_3 most of the nickel in the reaction is present as NiL_4.

$$HCN \ + \ NiL_4 \ \rightleftharpoons \ HNiL_3CN \ + \ L$$
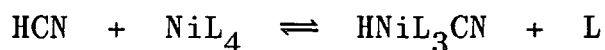
Scheme 11

Coordination of Lewis acid removes $HNiL_3CN$ from the equilibrium in Scheme 11, thus the concentration of nickel in the catalytic cycle is greatly increased and the overall rate of hydrocyanation is found to be close to first order in added BPh_3 [16].

The sterically more demanding $P(O-o-tolyl)_3$ ligand has a dissociation constant for loss of L from NiL_4 which is 10^8 times higher than that for the p-tolyl analogue [26]. Therefore, most of the nickel is present as NiL_3 before addition of BPh_3. Indeed BPh_3 slows down the reaction because $HNiL_3CN.BPh_3$ is slower to react than $HNiL_3CN$. The rate-accelerating effects of added $ZnCl_2$ or $AlCl_3$ have been related to their ability to catalyse carbon-carbon coupling reactions, in a similar manner to their effects on alkyl to carbonyl migration reactions [49].

1.4.7. Isotopic Labelling Experiments

Useful additional mechanistic information has recently been obtained by isotopic labelling experiments using DCN and $H^{13}CN$ in hydrocyanation reactions. The distribution of the isotopes determined by ^1H and ^{13}C N.M.R. spectroscopy provides details of the sense of addition of HCN as well as some useful information regarding various equilibria in the mechanism.

Two research groups in particular have studied the addition of HCN to monoolefins, and both have shown the addition to be stereospecifically cis [50,51].

Bäckval and Andell studied the reaction of DCN with 3-3-dimethyl-1-butene. They chose this olefin because the addition was known to be 99% regioselective to give the linear

nitrile [15]. The catalyst used was $Ni[P(OPh)_3]_4$ with $ZnCl_2$ in acetonitrile. The products from the addition of DCN to tert-BuCH=CHD were examined (<u>Scheme 12</u>).

+ ^{t}BuCH$_2$CHDCN

+ ^{t}BuCD$_2$CHDCN
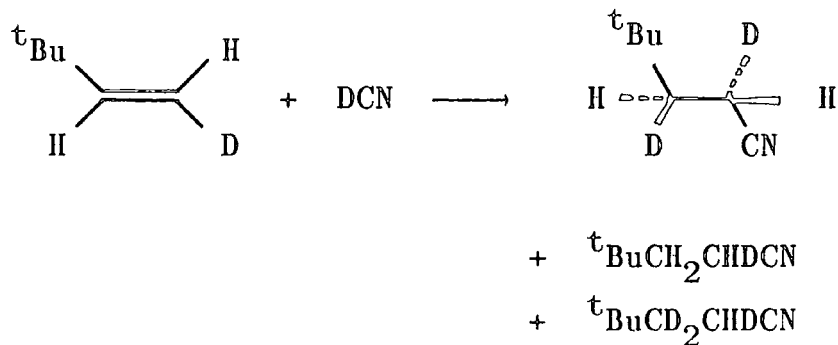
<u>Scheme 12</u>

The formation of the mono- and tri-deuterated products can be explained by H/D exchange between the alkene and DCN. No detectable exchange occurred at the terminal carbon atom of the alkene, so that studies of isotope effects could conveniently be carried out on non-deuterated alkene (vide infra). Jackson and co-workers [50] studied DCN addition to the same alkene catalysed by $Pd(DIOP)_2$. They established the stereochemistry of the HCN addition using the method of Whitesides and co-workers [52]. The nitrile from the reaction was reduced to the corresponding amine, which was in turn converted to a thiourea derivative. This sequence was used to ensure that the product adopted a staggered conformation. The value of $^3J_{^1H}$ coupling varies with dihedral angle, so the positions of the protons relative to each other was determined from ^1H N.M.R. spectra.

Both research groups found that the addition of HCN was cis

only. Jackson and Lovel compared the product to that obtained
by hydroformylation of the same alkene, and found that the
hydroformylation, although highly stereoselective, was not
stereospecific, unlike the hydrocyanation. The addition of DCN
to norbornene and norbornadiene catalysed by $Pd(DIOP)_2$ was shown
by [1]H N.M.R. to involve exclusively cis-exo addition, Scheme 13.
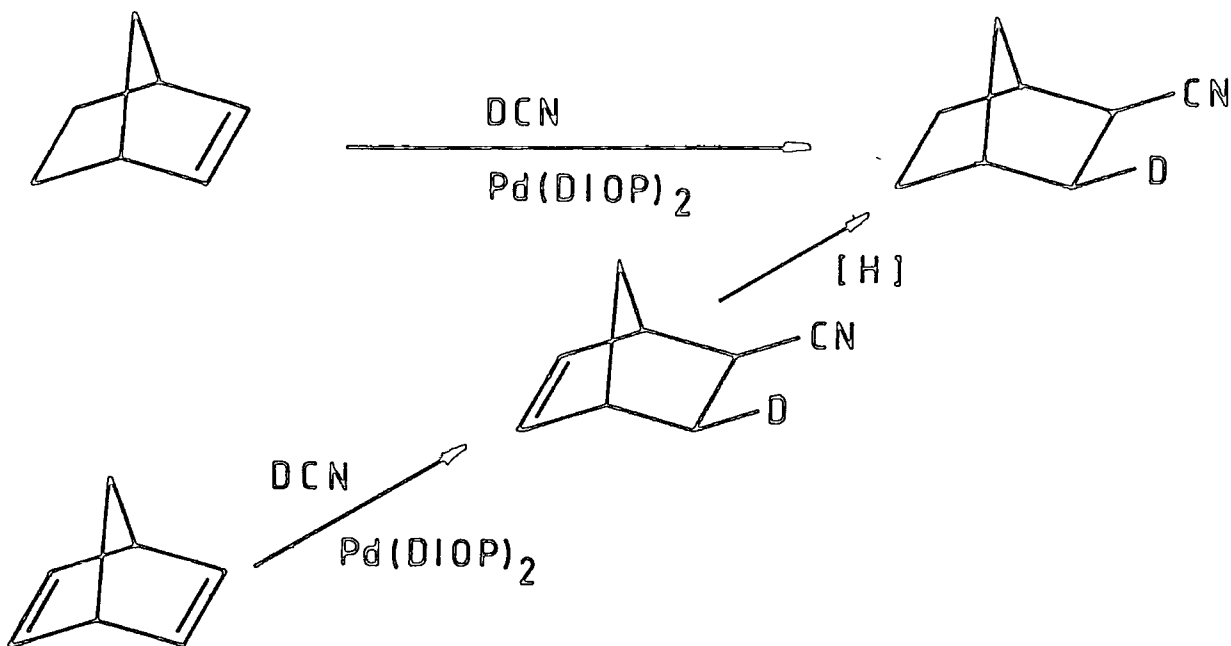
Scheme 13

Similarly addition of HCN and DCN to conformationally
biased cyclohexenes was shown to give only equatorial nitriles.

Bäckvall and Andell examined the isotope effect for
addition of HCN to both 3-3-dimethyl-1-butene and 1-3-cyclo-
hexadiene. The reaction of the monoene was complicated by the
fact that hydride addition to the alkene was reversible, whereas
the diene adds to nickelhydrido cyanide complexes irreversibly
to give stable π-allyl nickel cyanide complexes. The same
catalyst system was used for both the monoene and diene

experiments, with Lewis acid added as a promoter in the reaction of the monoene. The fact that exchange did not occur on the terminal carbon atom of the butene can be explained by the fact that the alkyl formed on addition of the butene to the nickel hydridocyanide complex bonds to the nickel only via the less hindered terminal carbon. Thus β hydride elimination will only allow exchange of H or D with the more hindered carbon. This fact allowed study of the isotope effect of HCN versus DCN addition using undeuterated olefin and DCN. In this reaction, three products were formed (Scheme 14). Initially only $RCH=CH_2$ and DCN are present; exchange of deuterium with alkene results in the formation of $RCD=CH_2$ and HCN. Both are formed in the same amounts, thus the missing components in reactions (c) and (d) appear in equal amounts at the same time. Therefore the isotope effect is equal to the ratio of product from reaction (c) to product from reaction (d). Note that addition of HCN to $RDC=CH_2$ does not affect this ratio (reaction b) as it removes the two missing components in equal amounts as if they had never been formed; also the secondary isotope effect of addition to $^tBuCD=CH_2$ compared to $^tBuCH=CH_2$ has been ignored.

They observed an unusually high deuterium isotope effect of 6.8 ± 1.0. If $k_2 \gg k_{-1}$ in Scheme 15 then the HCN and DCN would not equilibrate with $HNiL_3CN$ and $DNiL_3CN$, so the ratio of $HNiL_3CN$ to $DNiL_3CN$ would be higher than the ratio HCN to DCN exaggerating the isotope effect as $DNiL_3CN$ would not only react more slowly but would also be present in lower amounts.

(a)

$$R\text{--}C(H)(H)\text{=}C(H)(H) \; + \; DCN$$

(b)

$$R\text{--}C(H)(D)\text{=}C(H)(H) \; + \; HCN$$

$$\longrightarrow RCHDCH_2CN$$

(c)

$$R\text{--}C(H)(H)\text{=}C(H)(H) \; + \; HCN \longrightarrow RCH_2CH_2CN$$

(d)

$$R\text{--}C(H)(D)\text{=}C(H)(H) \; + \; DCN \longrightarrow RCD_2CH_2CN$$

<u>SCHEME 14</u>

$$HCN + NiL_3 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} HNiL_3CN \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} RNiL_nCN \xrightarrow{slow}$$
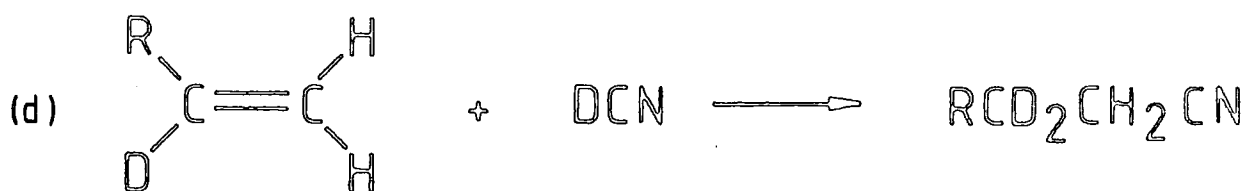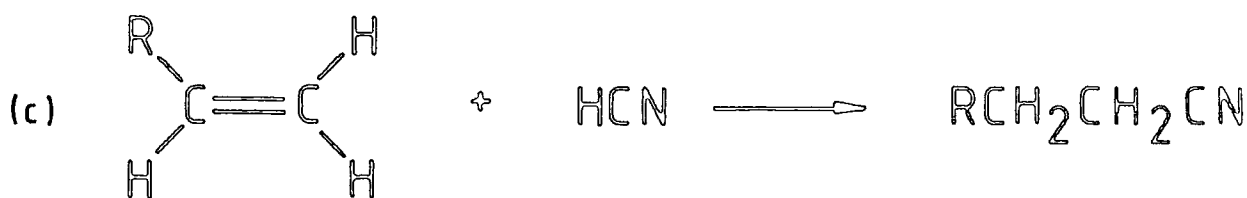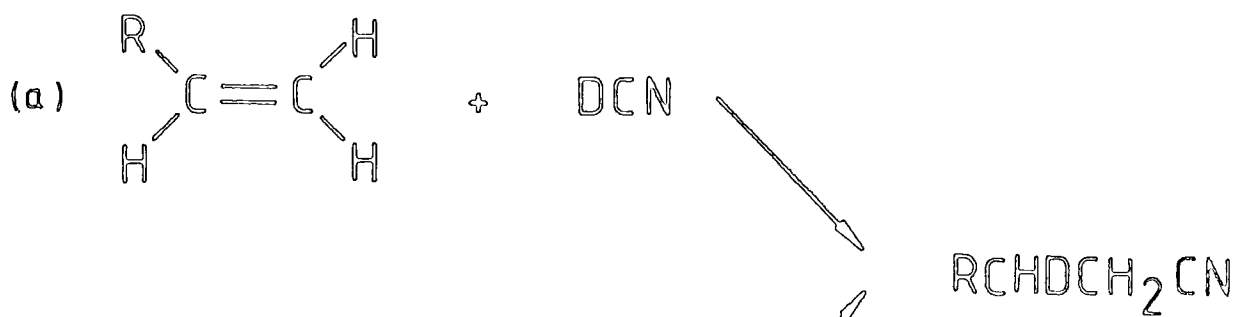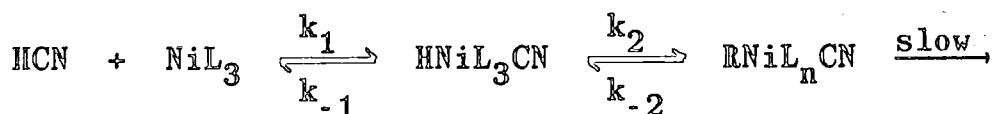
Scheme 15

However some equilibration does occur, therefore k_2 can only be moderately larger than k_{-1}. Bäckvall and Andell make no further suggestion as to the reason for the high isotope effect.

The measurement of the isotope effect for the diene is made easier by the irreversible addition to form the π-allyl nickel cyanide complex mentioned earlier. The observed value of 3.8 is consistent with addition of hydride to give the π-allyl occurring much more quickly than loss of HCN from the hydride to regenerate HCN and NiL_3: i.e. the isotope effect is probably related to the simple ratio k_{1H}/k_{1D} for the formation of the hydride vs. the deuteride.

Druliner and co-workers used addition of DCN and $H^{13}CN$ to various unsaturated nitriles relevant to the adiponitrile process to determine the sense of HCN addition. They also identified which olefins were precursors to dinitrile products, so that a clearer idea of isomerization mechanisms and reactions taking place was obtained [48].

1.4.8. The Use of N.M.R. Spectroscopy in Mechanistic Studies
       of Hydrocyanation

N.M.R. spectroscopy, particularly ^{1}H and [31]P N.M.R. is one of the most useful methods of analysing complexes and equilibria which may be of importance in the mechanism of homogeneous

transition metal catalysed hydrocyanations. The identification of reaction products with ^{1}H and [13]C N.M.R. is a routine step in examining the mechanism.

[31]P N.M.R. gives information via the phosphorus ligands present. In palladium complexes there is no coupling information from coupling of the phosphorus ([31]P I = $\frac{1}{2}$ natural abundance 100%) to the metal. This can be an advantage in that spectra are simpler, and a great amount of data can be obtained by observing chemical shifts and lineshapes.

The coordination of ligands to a metal causes a shift in the resonance position of the ligand; thus complex formation can be observed. The temperature dependence of lineshapes of free and complexed ligand signals with varying amounts of added free ligand provides information on the stability of complexes towards dissociation. Mann et al [53] discovered an empirical relationship between the coordination chemical shift $\Delta\delta$ and the position of the free phosphines for complexes of Rh, Ir, Ni(II), Pd(II) and Pt(II).

$$\Delta\delta = \delta_{complex} - \delta_{free\ ligand}$$

[31]P chemical shifts of coordinated ligand depend on the metal, the type of other coordinated ligands, the phosphine or phosphite itself; and the geometric arrangement of ligands. For d^8 square planar complexes the _trans_ influence of other coordinated ligands has been shown to affect the position of the ^{31}P chemical shift of coordinated phosphine ligands in the complexes

(trans)PdCl$_2$(Phosphine)(L)

An increase in the trans influence of L shifts the ^{31}P resonance to lower frequency [54].

The oxidation state of the central metal alters the ^{31}P chemical shift. In the Pt(II) complex PtCl$_2$(PEt$_3$)$_2$ the shift of the trans isomer is to higher frequency of the cis isomer, whereas the reverse is true for PtCl$_4$(PEt$_3$)$_2$.

It has been reported that for complexes differing only in the central metal, a shift of the ^{31}P resonance to low frequency is often observed as a given group of the periodic table is descended [55].

Care must be taken when trying to correlate ^{31}P chemical shifts to electronic and steric effects on the phosphorus ligand(s) under examination e.g. in the square planar cis and trans complexes of various phosphines MCl$_2$L$_2$, for M = Pd(II) δ^{31}P$_{cis}$ is at higher frequency than δ^{31}P$_{trans}$ [56], whereas for M = Pt(II) the reverse is true [57].

Ligand substitution to give known complexes, with previously determined ^{31}P N.M.R. spectral parameters, or the appearance of ^{31}P shifts of known species, are of use in elucidating structures of new complexes, or observing the reaction or decomposition pathways of relevant species.

Additional information is obtained from N.M.R. spectroscopy if ligands are coordinated to a magnetically active nucleus, e.g. Pt. Coordinated phosphorus ligands now couple with the 33% of magnetically active platinum. The magnitude of one bond

^{195}Pt to ^{31}P coupling constants $^{1}J_{Pt,P}$ can give further information on the coordination geometry of phosphine complexes, including information about the _trans_ influence mentioned above. This is an indirect effect; the trans ligand exerts an influence on the metal which in turn alters $^{1}J_{PtP}$. The more effectively the trans ligand competes for d electrons via π-bonding, the smaller $^{1}J_{PtP}$ becomes. Although this argument has been questioned [58], the comparison of coupling constants for various geometries and ligand types is very useful.

$^{1}J_{PPt}$ also provides an indication of the oxidation state of the central metal atom $^{1}J[Pt(IV),P] \leq {}^{1}J[Pt(II),P] \leq {}^{1}J[Pt(0),P]$ [55]. $^{1}J_{PtP}$ changes with the type of ligand; generally the greater the electronegativity of the groups attached to the phosphorus, the more s character in the phosphorus lone pair and the greater the coupling constant. For $PtCl_2(PR_nPh_{(3-n)})_2$ $^{1}J(M,P)$ increases with decreasing n.

Two bond through metal P,P coupling also occurs in phosphine complexes, although relatively little discussion of them appears in the literature (and values of $^{2}J_{(P,P)}$ are much less than $^{1}J_{(P,Pt)}$). $^{2}J_{(P,P)}$ coupling constants are at least useful in providing additional parameters to characterize N.M.R. observed complexes, particularly in palladium chemistry. The coupling constant may also be related to the coordination number of the metal, and in chelating biphosphine complexes, to the chelate bite angle, $P\hat{M}P$.

^{1}H N.M.R. spectroscopy utilized in conjunction with ^{31}P provides further mechanistic details. The observation of metal hydrides from their distinctive ^{1}H shift is one useful aspect.

These signals are sometimes difficult to observe due to their low intensity. Hydrides bound directly to platinum give $^1J(H,Pt)$ coupling information similar to that obtained for phosphorus ligands bound to platinum. ^1H N.M.R. shifts of easily observable groups on ligands e.g. methyl groups change on coordination and can add to the information obtained from ^{31}P N.M.R.

The coordination of species not observable by ^{31}P N.M.R. e.g. ethene and hydride can easily be monitored by ^1H N.M.R. The variation of lineshape with concentration and temperature gives details of exchange equilibria e.g. ^1H N.M.R. analysis of the olefinic protons of $(\eta^5-C_5H_5)$ Rh$(C_2H_4)_2$ 20 shows that the coordinated ethene rotates around the rhodium-ethene bond with a barrier to rotation of 15 Kcal mol^{-1}. The inner and outer olefinic protons H_i and H_0 can be distinguished in the ^1H N.M.R. [59].

20
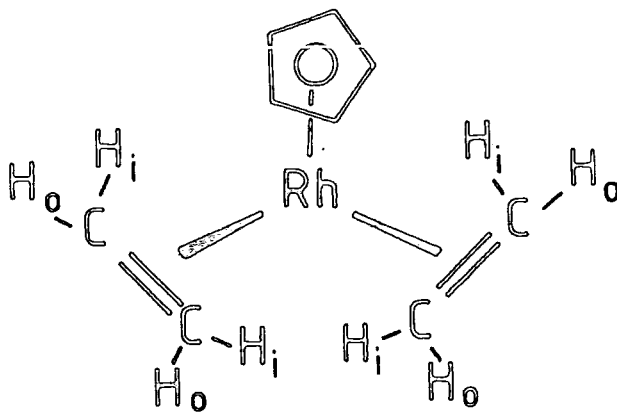
1.5. INTRODUCTION OF THE CYANIDE ION INTO ORGANIC SUBSTRATES

The cyanide ion is small and highly solvated in water. Before substitution can occur the attendant water molecules must be lost, limiting the nucleophilicity of the cyanide ion. A second problem arises when the substrate of interest is insoluble in water or is easily hydrolysed. Thus octyl bromide can be refluxed with aqueous sodium cyanide solution for two weeks and the only reaction which occurs is hydrolysis of the cyanide ion [60].

The classical solution to the problem is the use of a solvent in which both components dissolve e.g. an alcohol, which is however a compromise as the substrate may be only sparingly soluble, and the cyanide ion will still be solvated to some extent. The reaction of octyl bromide and sodium cyanide in refluxing ethanol gives a 60% yield of octyl cyanide after 35 hours.

More recently dipolar aprotic solvents have been introduced e.g. DMSO, DMF and CH_3CN. These solvents preferentially solvate the cation, so that the anion is rendered more reactive as desolvating is not necessary prior to reaction. The octyl bromide/sodium cyanide reaction proceeds to completion after $\frac{1}{2}$ hour at $150^{\circ}C$ in DMF [61]. The drawbacks of dipolar aprotic solvents are their relative expense, the inherent difficulties in working with them and difficulties in purifying and drying them. The work-up of reactions is also difficult using these solvents e.g. the high boiling point of DMSO.

Finally cyanide ion can be solubilized in solvents of low polarity by pairing it with a large polarizable cation (usually

a quaternary ammonium or phosphonium salt). One of the most convenient and widely used of such solubilization methods involves 'phase transfer catalysis', in which two immiscible phases are present. One phase (usually aqueous) contains an excess of the nucleophile to be reacted with the organic substrate in the second phase. The phase transfer catalyst is soluble in both phases and on addition to the system, can transport the nucleophile into the organic phase in the form of an ion pair, where the nucleophilic displacement reaction can occur. The nucleofuge is transported back into the aqueous phase by the catalyst, where ion exchange with the nucleophile allows the cycle to continue.

One of the earliest phase transfer reactions to be studied was the reaction of alkyl halides with cyanide catalysed by tetra-alkyl ammonium or phosphonium salts in 1970 by Starks [60]. The diagram of Starks representing the catalytic cycle is shown in Scheme 16. Subsequent investigations [60,62,63,64] have shown the reaction to be a true phase transfer reaction,

QNu + R-X ⟶ RNu + QX   Organic Phase

QNu + MX ⇌ MNu + QX   Aqueous Phase
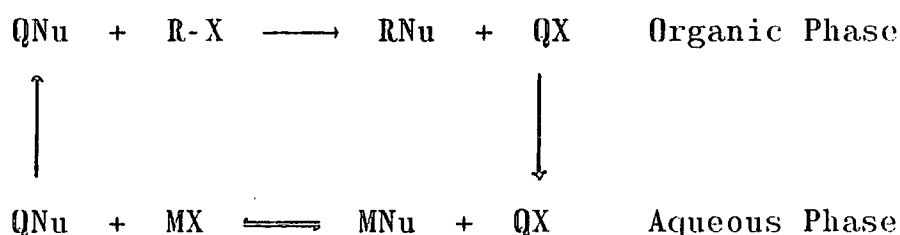
Scheme 16

not involving micelle formation. Thus some poor surfactants (e.g. tetradodecylammonium salts), are effective phase transfer catalysts [64], and the rate of reaction is independent of the

stirring speed beyond a certain minimum value sufficient to remove any concentration gradients within either of the layers.

It has been shown that the actual rate determining nucleophilic displacement reaction takes place in the organic phase, [60,65] and is first order in alkyl halide and in catalyst [60].

Examples of commonly used phase transfer catalysts includes hexadecyltributylphosphonium bromide, $C_{16}H_{33}(But)_3\overset{+}{P}Br^-$ and tetrabutylammonium bromide. A study of the relative efficiencies of a range of catalysts [65] showed the following general trends for the cation:

(i)   larger quaternary ions are better catalysts;

(ii)   symmetrical ions are better than those with only one long chain;

(iii)   phosphonium ions are more effective and thermally stable than the corresponding ammonium catalysts;

(iv)   ions containing alkyl rather than aryl groups are better catalysts.

The quaternary ions will tend to pair preferentially with the softest anion in the system (soft in the HSAB sense), thus if the leaving group is 'softer' than the nucleophile, the reaction will be slowed down. In some cases the reaction can be stopped completely. This often happens if iodide ions are present. Such problems may be partly overcome by the use of excess nucleophile; concentrated aqueous solutions [66] and/or replenishment of nucleophile by repeatedly replacing the aqueous layer with fresh solution.

Crown ethers function as phase transfer catalysts by complexing with alkali metal carbons, rendering alkali metal salts soluble in organic media [67]. However crown ethers are highly toxic.

To sum up, the advantages of phase transfer techniques include improved yields and reaction rates, suppression of side reactions, lower temperatures can often be used and the 'work-up' is often more simple. Some reactions accomplished using phase transfer techniques do not otherwise occur, also the selectivity and product ratio of a particular reaction can be modified by phase transfer techniques. On an industrial scale, phase transfer catalysts would be cheaper to use than conventional methods as expensive anhydrous aprotic solvents or crown ether ligands are not required.

Liquid/liquid phase transfer techniques can be used for reactions of some hydrolysis-sensitive substrates, [68]. However, water molecules do accompany the ion pair transported into the organic phase. Starks has reported that four to five molecules accompany each cyanide ion into the organic phase, [64]. It appears that the amount of water present in the organic phase depends on the inorganic salt, the quaternary ion used and its concentration, [64,65]. The effect of water in the system depends on the reaction taking place. Thus nitrile formation is unaffected [69], whereas dry tetrabutylammonium thiophenoxide dissolved in anhydrous benzene was around ten times more reactive than the same ion pair added to a benzene-water mixture [65].

Solid/liquid phase transfer catalysis is possible with

crown ethers, although a trace of water is perhaps present in most cases [70].

The ideal reactant is thus a previously prepared dry solution of the anhydrous 'onium salt of the desired nucleophile in an organic solvent. Such a solution would be more reactive in general than the same ions under phase transfer conditions, and would perhaps allow reactions with more hydrolysis-sensitive substrates. The study presented in this thesis has also shown that product ratios can be altered by the use of anhydrous salts. Unfortunately, in the case of most desired nucleophiles, (including cyanide), the preparation of the 'onium salt involves an extra preparative step, i.e. the 'onium salts rarely initially matches with the desired anion. A second problem, particularly with cyanide and fluoride salts currently available is that the salts are very hygroscopic and difficult to handle. Some homogeneous reactions of tetra-alkylammonium cyanides have been described in the literature [62,71,72,73]. Thus tetrabutylammonium cyanide reacts with n-heptylcyanide in 30 minutes at 20°C and with hydrolysis sensitive phenylchloroformate in methylene chloride to give the corresponding cyanoformate, [72].

In 1977 Martinsen and Songstad reported the preparation and properties of some salts of the bis(triphenylphosphine)iminium salts $[(Ph_3P)_2N]X^{\dagger}$, hereafter abbreviated [PNP]X. They noted

---

[†] Bis(triphenylphosphine)iminium ion is the usual name for this ion, but since this ion is fundamentally not an iminium ion, various other names have been suggested and used. Chemical Abstracts recommends the cumbersome triphenyl(P,P,P-triphenyl-phosphine imidato-N)phosphorus(1+). The Aldrich Chemical Company use bis(triphenylphosphoranylidene)ammonium ion. Other names such as hexaphenyldiphosphazenium ion, bistriphenylphosphine nitride ion, μ-nitrido-bis(triphenyl phosphorus)(1+) ion and bis(triphenylphosphoranylidene)-iminium ion are also used. To avoid confusion the abbreviation $[PNP]^{+}$ is used here throughout. Some authors use PPN^{+}, but this abbreviation should be avoided.

the "apparently exceptional hydrophobic nature" of the $[PNP]^+$ ion and the fact that all known salts, including the cyanide, were non-hygroscopic, [74]. The related tetraphenyl-phosphonium and tetraphenylarsonium salts in contrast are known to pick up 1 to 3 mol of water [75]. They also suggested that salts of $[PNP]^+$ may be useful for performing homogeneous reactions. The aim of the study presented was to determine the synthetic utility of $[PNP]^+$ salts for reactions involving the cyanide ion in both phase transfer and stoichiometric systems.

REFERENCES

1. M.F. Semmelhack, Pure Appl. Chem., 53, 2379, (1981).

2. (a) G.R. Coraor and W.Z. Heldt, U.S. Pat., 2,904,581.
    (1959); Chem. Abstr., 54, 4393, (1969).
    (b) Brit. Pat., 845,086.
    (c) Can. Pat., 628, 973.

3. (a) W.C. Drinkard Jr. and R.V. Lindsey, Brit. Pat.,
    1,104,140 (1968); Chem. Abstr., 68, 77795, (1968).
    (b) U.S. Pat., 3,496,215, (1970).
    (c) Belg. Pat., 698,333.
    (d) Neth. Pat., 68 05,556.

4. (a) W.C. Drinkard Jr. and R.V. Lindsey, Ger. Offen.,
    1,806,098, (1969); Chem. Abstr., 71, 49343, (1969).
    (b) Belg. Pat., 723,128.
    (c) Neth. Pat., 68 15,487.

5. P. Arthur Jr. and B.C. Pratt, U.S. Pat., 2,571,099, (1951);
    Chem. Abstr., 46, 3068.

6. G.W. Parshall, "Homogeneous Catalysis", p. 219, Wiley, New
    York, (1980).

7. (a) P. Arthur Jr., D.C. England, B.C. Pratt and
    G.M. Whittman, J. Am. Chem. Soc., 76, 5364, (1954).
    (b) P. Arthur Jr. and B.C. Pratt, U.S. Pat., 2,666,780,
    (1954); Chem. Abstr., 49, 1776a, (1955).
    (c) P. Arthur Jr. and B.C. Pratt, U.S. Pat., 2,666,748,
    (1954); Chem. Abstr., 49, 1774c, (1955).

8. (a) W.C. Drinkard Jr. and B.W. Taylor, Belg. Pat., 727,382.
    (b) Neth. Pat., 68 15,812.

9.   (a) W.C. Drinkard Jr., U.S. Pat., 3,496,218.

      (b) Fr. Pat., 1,544,658.

      (c) Neth. Pat., 67 06,555.

      (d) Brit. Pat., 1,112,539; Chem. Abstr., 69, 26810, (1968).

      (e) Belg. Pat., 698,332.

10.   (a) D.Y. Waddan, Ger. Offen., 2,344,767, (1974); Chem. Abstr., 80, 145481u, (1974).

      (b) D.Y. Waddan and G.R. Crooks, Ger. Offen., 2,450,863, (1975); Chem. Abstr., 83, 58183s, (1975).

      (c) D.Y. Waddan, Ger. Offen., 2,336,852, (1974); Chem. Abstr., 80, 120342m, (1974).

      (d) D.D. Coffman, L.F. Salisbury and N.D. Scott, U.S. Pat., 2,509,859, (1950); Chem. Abstr., 44, 8361c, (1950).

      (e) R.J. Benzie and D.Y. Waddan, Ger. Offen., 2,805,760, (1978); Chem. Abstr., 89, 214924r, (1978).

      (f) R.J. Benzie and D.Y. Waddan, Ger. Offen., 2,812,151, (1978).

11.   C.A. Tolman, R.J. McKinney, W.C. Seidel, J.D. Druliner and W.R. Stevens, Adv. Catal., 33, 1, (1985).

12.   A.J. Hubert and E. Puentes, "Catalysis in C1 Chemistry" (W. Keim, ed.), pp. 219-242, Reidel, Dordrecht, (1983).

13.   E. Puentes, A.F. Noels, R. Warin, A.J. Hubert, Ph. Teyssié and D.Y. Waddan, J. Mol. Catal., 31, 183-190, (1985).

14.   (a) U.S. Pat., 3,778,462, (1973).

      (b) H.E. Swift and C.Y. Wu, U.S. Pat., 4,215,068, (1980); Chem. Abstr., 93, 238927c, (1980).

15.   B.W. Taylor and H.E. Swift, J. Catal., 26, 254-60, (1972).

16. C.A. Tolman, W.C. Seidel, J.D. Druliner and P.J. Domaille. Organometallics., 3, 33-38, (1984).

17. W.R. Jackson and C.G. Lovel, Aust. J. Chem., 35, 2053-67, (1982).

18. W.A. Nugent and R.J. McKinney, J. Org. Chem., 50, 5370-2, (1985).

19. (a) E.S. Brown and E.A. Rick, J. Chem. Soc. Chem. Commun., 112, (1969).

    (b) E.S. Brown and E.A. Rick, Amer. Chem. Soc., Div. Petrol. Chem. Prepr., 14, 1329, (1969).

20. (a) W.R. Jackson and P.S. Elmes, J. Amer. Chem. Soc., 101. 6128, (1979).

    (b) P.S. Elmes and W.R. Jackson, Ann. N.Y. Acad. Sci., 333. 225, (1980).

21. W.R. Jackson and P.S. Elmes, Aust. J. Chem., 35, 2041-51, (1982).

22. (a) W.R. Jackson and C.G. Lovel, Aust. J. Chem., 35, 2069-75, (1982).

    (b) R.J. Thomson, W.R. Jackson, D. Haarburger, E.I. Klabunovsky and V.A. Pavlov, Aust. J. Chem., 40, 1083-106, (1987).

23. C.A. Tolman, J. Amer. Chem. Soc., 92, 2953, (1970).

24. C.A. Tolman, J. Amer. Chem. Soc., 92, 2956, (1970).

25. L.W. Gosser and C.A. Tolman, Inorg. Chem., 9, 2350, (1970).

26. C.A. Tolman, W.C. Seidel and L.W. Gosser, J. Amer. Chem. Soc., 96, 53, (1974).

27. C.A. Tolman, D.W. Reutter and W.C. Seidel, J. Organomet. Chem., 117, C30, (1976).

28. C.A. Tolman, Chem. Rev., 77, 313, (1976).

29. C.A. Tolman, Inorg. Chem., 10, 1540, (1971).

30. W.C. Seidel and C.A. Tolman, Inorg. Chem., 9, 2354, (1970).

31. C.A. Tolman and W.C. Seidel, J. Amer. Chem. Soc., 96, 2774, (1974).

32. C.A. Tolman, J. Am. Chem. Soc., 96, 2780, (1974).

33. C.A. Tolman, W.M. Riggs, W.J. Linn, C.M. King and R.C. West, Inorg. Chem., 12, 2770, (1973).

34. L. Guggenberger, Inorg. Chem., 12, 499, (1973).

35. C.A. Tolman, A.D. English and L.E. Manzer, Inorg. Chem., 14, 2353, (1975).

36. F. Cariati, R. Ugo and F. Bonati, Inorg. Chem., 5, 1128, (1966).

37. W.C. Drinkard, D.R. Eaton, J.P. Jesson and R.V. Lindsey Jr., Inorg. Chem., 9, 392, (1970).

38. R.A. Schunn, Inorg. Chem., 9, 394, (1970).

39. (a) C. Corain, P. Rigo and G. Favero, Inorg. Chem., 10, 2329, (1971).

    (b) P. Rigo, B. Corain and A. Turco, Inorg. Chem., 7, 1623, (1968).

40. J.D. Druliner, A.D. English, J.P. Jesson, P. Meakin and C.A. Tolman, J. Amer. Chem. Soc., 98, 2156, (1976).

41. C.A. Tolman, J. Amer. Chem. Soc., 94, 2994, (1972).

42. C.A. Tolman, J. Amer. Chem. Soc., 92, 6777, (1970).

43. C.A. Tolman, W.C. Seidel and D.H. Gerlach, J. Amer. Chem. Soc., 94, 2669, (1972).

44. R.J. McKinney and D.C. Roe, J. Amer. Chem. Soc., 108, 5167-5173, (1986).

45. R.J. McKinney and D.C. Roe, J. Amer. Chem. Soc., 107, 261-262, (1985).

46. (a) W.C. Seidel and C.A. Tolman, Ann. N.Y. Acad. Sci., 415, 201, (1983).

    (b) E.M. Campi, P.S. Elmes, W.R. Jackson, C.G. Lovel and M.K.S. Probert, Aust. J. Chem., 40, 1053-61, (1987).

47. K. Tatsumi, A. Nakamura, S. Korniya, A. Yamamoto and T. Yamamoto, J. Amer. Chem. Soc., 106, 8181, (1984).

48. J.D. Druliner, Organometallics., 3, 205-8, (1984).

49. S.B. Butts, E.M. Holt, S.H. Strauss, N.W. Alcock, R.E. Stinson and D.F. Shriver, J. Amer. Chem. Soc., 101, 5864, (1979).

50. W.R. Jackson and C.G. Lovel, Aust. J. Chem., 35, 2053-67, (1982).

51. J.E. Backvall and O.S. Andell, Organometallics., 5, 2350-55, (1986).

52. G.M. Whitesides, J.P. Sevenair and R.W. Goetz, J. Amer. Chem. Soc., 89, 1135, (1967).

53. R.E. Mann, C. Masters, B.L. Shaw, R.M. Slade and R.E. Stainbank, Inorg. Nucl. Chem. Lett., 7, 881, (1971).

54. G. Balimann and P.S. Pregosin, J. Magn. Reson., 22, 235, (1976).

55. "^{31}P and ^{13}C N.M.R. of Transition Metal Complexes", P.S. Pregosin, R.W. Kunz, Springer-Verlag, New York, (1979).

56. S.O. Grim and R.L. Keiter, Inorg. Chim. Acta, 4, 56, (1970).

57. S.O. Grim, R.L. Keiter and W. McFarlane, Inorg. Chem., 14, 1456, (1975).

58. P.I. Van Bliet, J. Kuyper and K. Vrieze, J. Organomet. Chem., 122, 99, (1976).

59. E. Cramer, J. Amer. Chem. Soc., 86, 217, (1964).

60. C.M. Starks, J. Amer. Chem. Soc., 93, 195-99, (1971).

61. A.I. Vogel, "A Textbook of Practical Organic Chemistry", 4th Edition, Longman, London, (1978).

62. W.P. Weber and G.W. Gokel, "Phase Transfer Catalysis in Organic Synthesis", Springer-Verlag, New York, (1977).

63. E.V. Dehmlow and S.S. Dehmlow, "Phase Transfer Catalysis". Monographs in Modern Chemistry, 11, Verlag Chemie, Florida, (1980).

64. C.M. Starks, J. Amer. Chem. Soc., 95, 3613-17, (1973).

65. A.W. Herriott and D. Picker, J. Amer. Chem. Soc., 97, 2345, (1975).

66. Y. Sasson and A.Z. Hayder, J. Chem. Soc. Chem. Commun., 1347, (1983).

67. R. Chenevert, R. Plante and N. Voyer, Synthetic Commun., 13, 405, (1983).

68. K.E. Koenig and W.P. Weber, Tet. Lett., 2275-78, (1974).

69. J.W. Zubrick, B.I. Dunbar and H.D. Durst, Tet. Lett., 71, (1975).

70. M.E. Childs and W.P. Weber, J. Org. Chem., 41, 3486, (1976).

71. G. Simchen and H. Kobler, Synthesis, 605, (1975).

72. H. Kobler, K.H. Schuster and G. Simchen, Liebigs. Ann. Chem., 1940, (1978).

73. D.A. White and M.M. Baizer, <u>J. Chem. Soc. Perkin I</u>, 2230, (1973).

74. A. Martinsen and J. Songstad, <u>Acta Chem. Scand.</u>, <u>A31</u>, 645-50, (1977).

75. K.W. Loach, <u>Anal. Chim. Acta</u>, <u>44</u>, 323, (1969).

CHAPTER 2

PALLADIUM CATALYSED ASYMMETRIC HYDROCYANATIONS

2.1. INTRODUCTION

The formation of chiral compounds from a reaction is becoming increasingly important in organic chemistry, as different enantiomers often have quite different biological properties. For example racemic lysine cannot be used as an animal feedstock, because one enantiomer (d-lysine) is toxic. Asymmetric catalysis obviates the need for optically active starting materials, and reagents for the separation of enantiomers. Furthermore, catalytic reactions are usually the most cost effective way of performing chemical reactions, so that asymmetric catalytic reactions are of considerable importance.

Homogeneous catalysis using soluble transition metal catalysts is a relatively new technique. Interest was stimulated around twenty years ago by Wilkinson and Osborn who introduced rhodium tris(triphenylphosphine)chloride as a catalyst for the hydrogenation of alkenes and alkynes [1,2]. Homogeneous asymmetric catalyst systems based on Wilkinson's catalyst appeared soon after, first with chiral phosphine ligands [3] e.g. methylphenylpropylphosphine. Using the rhodium complex of this chiral phosphine α-phenylacrylic acid was reduced to optically active (+)hydratropic acid in a 15% optical yield (Scheme 1).

Developments in phosphine design and particularly the implementation of chiral biphosphines, improved optical yields. The rhodium complex of DIPAMP, 1, has been used by Monsanto to effect an asymmetric hydrogenation on an industrial scale, [4]. This involves the manufacture of L-Dopa, used in the treatment

$$\underset{HOOC}{\overset{Ph}{\diagdown}} C = CH_2 \quad \xrightarrow[\text{CH}_3\text{OH/H}_2,\,60°\text{C},\,20\text{atm.}]{\text{RhL}_3\text{Cl}_3\,,\ \text{Et}_3\text{N}\,,\ \text{C}_6\text{H}_6} \quad \underset{HOOC}{\overset{Ph}{\diagdown}} \overset{CH_3}{\underset{H}{C}}$$

$$L \quad = \quad n-C_3H_7 \overset{..}{P} \diagdown \overset{CH_3}{\underset{C_6H_5}{}}$$
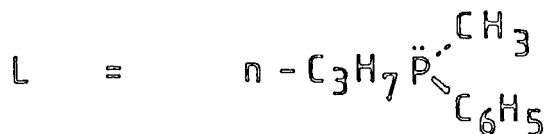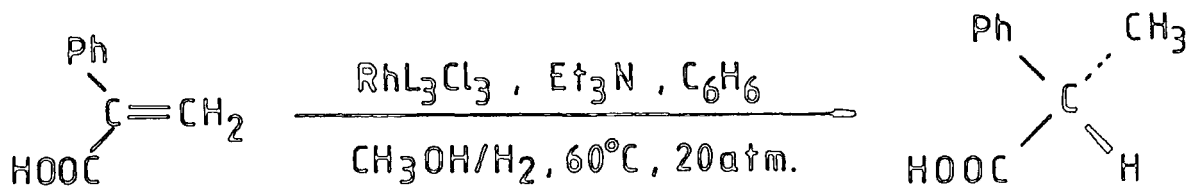
Scheme 1
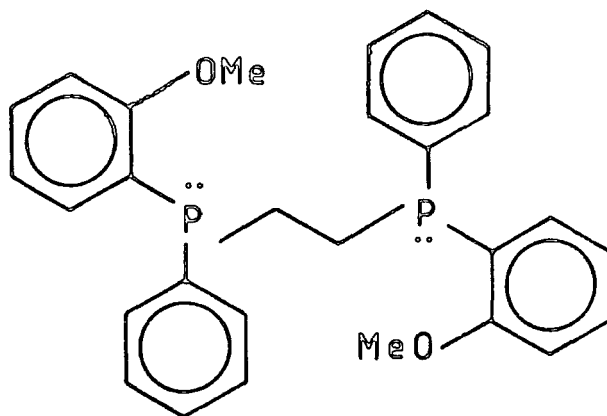
1

of Parkinson's disease, with 94% optical yield and a 10^4 to 1

substrate to catalyst ratio.

Later it was discovered that the chiral centre conferring

asymmetry on the products did not have to be so close to the

central metal atom, i.e. ligands possessing chiral centres at

* Enantiomeric purity or excess is the percentage excess of one
enantiomer over the other, i.e. a mixture containing 55% of
one enantiomer and 45% of the other would have 10% e.e.
Enantiomeric excess may be determined directly using N.M.R..
G.L.C. or H.P.L.C. analysis. The optical yield is the ratio
of the observed specific rotation to the specific rotation of
the pure enantiomer and corresponds to the enantiomeric
excess.

carbon could be used. The great advantage over chiral
phosphorus ligands, which invariably required a separation of
enantiomers at some stage, was that cheap, naturally occurring
chiral starting materials could be used e.g. menthol, camphor.
lactic acid, tartaric acid, ℓ-hydroxyproline, sugars, etc. The
use of tartaric acid, for example, was first reported in 1971
[5], for the synthesis of the chiral biphosphine, DIOP.

Atropisomeric ligands which are chiral by virtue of
restricted rotation around a carbon-carbon bond joining biaryl
systems have recently shown promise and give good optical yields
in hydrogenation reactions [6,7,8].

Optical and preparative yields for hydrogenations are now
very high, ($\geq$ 95%), and the mechanism has been thoroughly
investigated. However for carbon-carbon bond-forming reactions.
optical yields in catalytic organometallic reactions available
are often less spectacular. Reactions studied include
hydroformylation, cyclopropanation, Grignard (alkyl-vinyl) cross
coupling, olefin dimerization, allylic alkylation and
hydrocyanation.

Asymmetric hydrocyanation has only been reported with any
significant asymmetric induction in one system [9]. The
reported optical yields (vide infra) are shown in this work to
be less than half that originally claimed [10].

The mechanism of hydrocyanations in general had been little
studied, with no published work on the mechanism of asymmetric
hydrocyanation to date. Thus an investigation was undertaken to
study the catalysis of HCN addition to alkenes.

The first step was a search for better cheaper asymmetric

ligands. Chiral phosphinites $R_1R_2R_3COPPh_2$ or diphosphinites are more easily prepared than the corresponding phosphines. Both ligands can be prepared from the related diols.

The use of rhodium complexes of phosphinites to effect asymmetric hydrogenations was first reported in 1975 [11]. Chiral diphosphinite rhodium complexes were prepared from d-trans-1,2-bis(diphenylphosphinoxy)cyclopentane 2a, and (+)trans-1,2-bis(diphenylphosphinoxy)cyclohexane 2b.
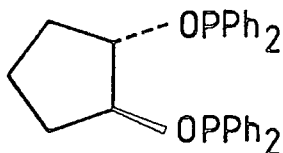
2a
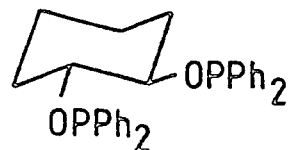
2b

The more rigid cyclopentane derived ligand gave better results than the cyclohexane based ligand; both catalysts were efficient, and in certain cases superior to the chelating asymmetric biphosphine DIOP. For example when the ligands were used in the hydrogenation of ethylstyrene catalysed by rhodium, the optical yields were 60, 30 and 24% for the cyclopentane, cyclohexane derivative and DIOP respectively, [12]. These results have not been reproduced however.

The use of sugar as starting materials has been investigated, [13]. One such 1,2-biphosphinite 4, is prepared by the action of Ph_2PCl on the sugar 3. The air stable ligand gave 100% conversion with 80% optical yield in the reduction of substrates containing an acetamido group. Reactions were

3

4

5
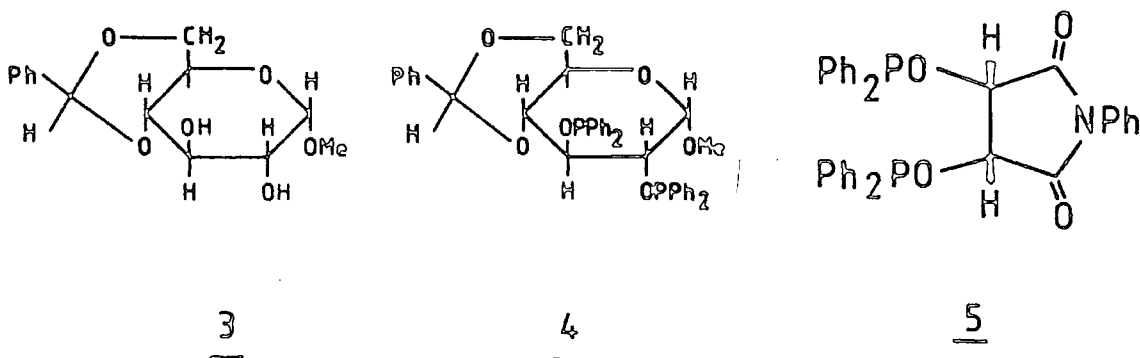
carried out in ethanol. Substrates without acetamido groups were not reduced, suggesting coordination of both olefin and acetamido moiety to rhodium during the reaction.

Several other 1,2-diphosphinites from sugars have been tested, [14]. Jackson and Thompson synthesised six ligands derived from α and β-D-glucose, β-D-galactose and D-xylose. The rhodium complexes of these ligands gave complete reduction of substrates containing acetamido groups, the products having optical yields of up to 80%.

Johnson and co-workers compared the activity of phosphinites with phosphines prepared from the same diol intermediates [15]. They compared three phosphine/phosphinite pairs: two were derived from sugars, and one from the diol precursor of camphos shown below. It was found that the phosphines were generally better for substances containing an acetamido or carboxylic acid group, whereas phosphinites were superior when ester groups were present in the substrate [16]. It is worth noting that the chelate ring size in the phosphinites is two atoms bigger than in the equivalent
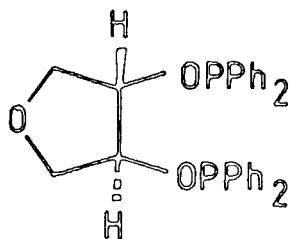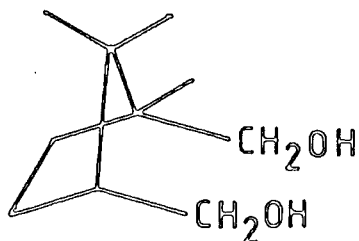
DIPHIN

phosphine complexes, and this is expected to affect both the reactivity and efficiency of the catalyst.

The phosphinite equivalent of DIOP and another bis-1,2-diphosphinite also derived from tartaric acid 5 were tested as ligands for asymmetric hydrogenation [17]. Ligand 5 was better than the DIOP analogue presumably because of the more rigid seven membered chelate ring formed on metal complexation. The hydrogenations were carried out in absolute ethanol due to the low solubility of the complexes in other solvents. When the course of the reaction was monitored, (the reduction by U.V. spectroscopy and the asymmetric induction by polarimetry) it was found that asymmetric induction stopped a long time before completion of reduction. Bourson and Oliveros [17] suggested that this was due to a change in the catalyst, possibly by alcoholysis of the ligand. This suggestion was supported by the observation that 5 may be converted back to its diol precursor by boiling for a short time in ethanol.

Petit and co-workers [18] tested aminophosphine phosphinites derived from aminoalcohols as ligands for hydro-silylation, hydrogenation, hydroformylation and cyclo and codimerization of 1,3-diolefins.

The only phosphinite tested for hydrocyanation was DIPHIN

[19]. It gave moderate yields.

2.2. THE SYNTHESIS OF CHIRAL PHOSPHINITES

The first step in the study was to attempt to synthesise various chiral phosphinite ligands. Such ligands are readily prepared from simple alcohols or diols. Furthermore, it has been clearly demonstrated that the related aryl phosphites are excellent ligands in nickel catalysed hydrocyanations. Four alcohols were chosen for initial study. Menthol 6a and neomenthol 6b because of their cheapness and natural chirality. Neomenthyldiphenylphosphine is a good ligand for asymmetric hydrogenations using its rhodium complex. For example the Rh(I) complex of neomenthyldiphenylphosphine catalyses the reduction of Z-3,7-dimethylocta-2,6-dienoic acid to 7-dimethyloct-6-enoic acid to give a product with 77% e.e. [20]. Chelating phosphines are more efficient ligands for catalysis of hydrocyanations than monophosphines [9]. Therefore two diols, both available as racemates, and in enantiomerically pure form, were selected in order to investigate chelating phosphinites. The diphosphinite of binaphthol, 7, had been reported in a comm018nciation [6]. Butane-2,3-diol, 8, appeared a simple source of a chiral chelating diphosphinite which would have the same chelate ring size as DIOP.

Phosphinites are generally prepared by the action of a phosphorus electrophile on an alcohol. Chlorodiphenylphosphine is most commonly used. The hydrogen chloride formed in the reaction is neutralized by a base, usually pyridine, which is often used as the solvent.
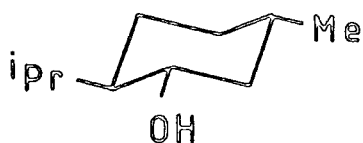
6a
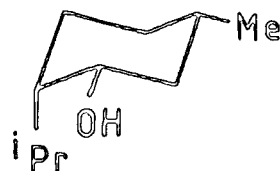
6b
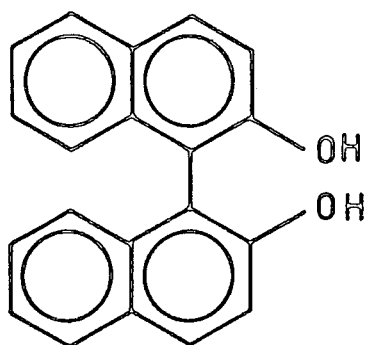
7
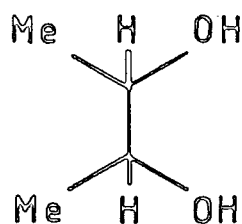
8

2.2.1. Preparation of Diphenylmenthylphosphinite

Brunner had reported the synthesis of mentholphosphinite in 1977. He claimed that it was unstable above -20°C [21]. This was found not to be the case. A number of techniques for preparing and working up diphenylmenthylphosphinite were attempted, the simplest of which proved to give the highest isolated yields (> 95%), and the purest product (Scheme 2).

A solution of the phosphine in THF was added dropwise to a solution of menthol and triethylamine in THF, cooled to -10°C. The reaction is exothermic, and the mixture was stirred for four

$$\text{iPr} \overset{}{\underset{OH}{\diagdown}} + Ph_2PCl \xrightarrow[\text{0°C, 4hrs, N}_2]{\text{THF, Et}_3N} \text{iPr} \overset{}{\underset{OPPh_2}{\diagdown}} + Et_3\overset{+}{N}HCl^-$$
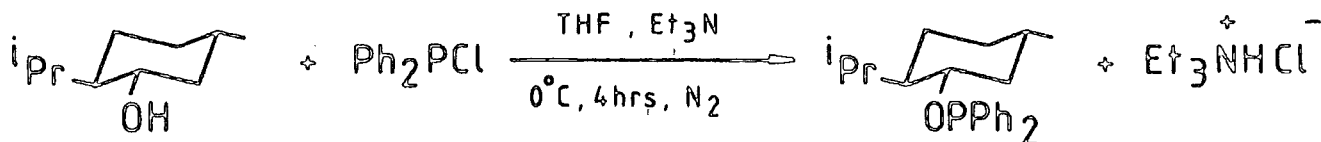
Scheme 2

hours at 0°C. The precipitate of amine salt was filtered off
and the solvent removed in vacuo. The remaining oil
crystallized over 1-3 days and was used in this form. (This
practice is found in other literature procedures e.g. [16].)

Phosphinite esters are susceptible to decomposition in a
number of ways, (<u>Scheme 3</u>). As with most phosphorus(III)

$$R_2\overset{O}{\overset{\|}{P}}R'$$

$$R_2POR' \xrightarrow{\Delta} \quad \xrightarrow{R''OH} R_2POR'' + R'OH$$

$$R_2\overset{O}{\overset{\|}{P}}OR' \xleftarrow{\frac{1}{2}O_2} R_2POR' \xrightarrow{H_2O}$$

$$\xrightarrow{-ROH} R_2POH \rightleftharpoons R_2\overset{O}{\overset{\|}{P}}H$$
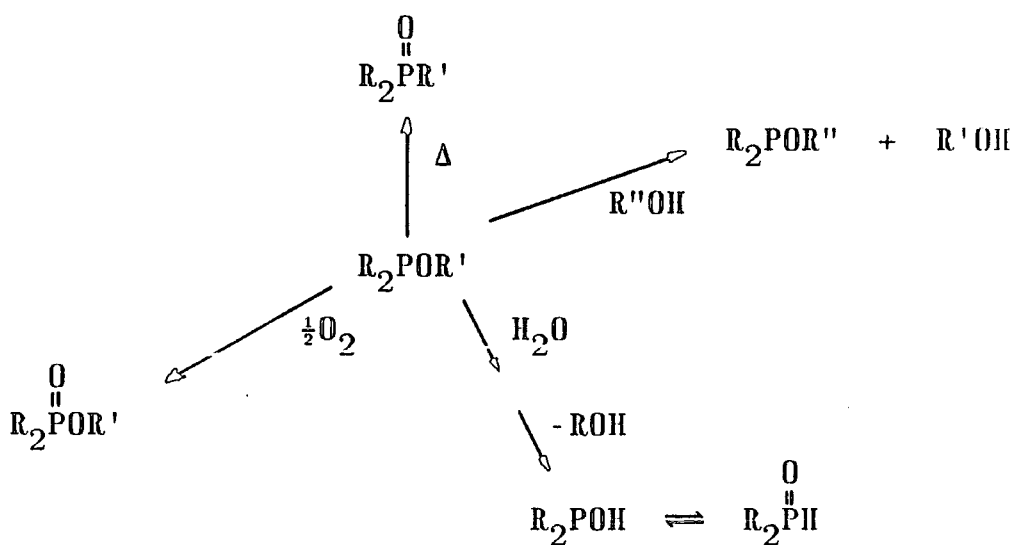
Scheme 3

compounds, phosphinites are relatively unstable in air, being
oxidised to phosphinates. The preparation and handling of these
compounds was accordingly carried out under nitrogen or argon.
Phosphinites may also undergo trans-esterification reactions
with primary, secondary and tertiary alcohols.

In view of the reported instability of diphenylmenthyl-phosphinite it is worth reviewing the evidence for the formulation of this product as Ph_2P-O-menthyl, rather than any of the decomposition products mentioned above.

The most compelling evidence is the [31]P N.M.R. shift of a solution of the product in dichloromethane. Referring to tables of ^{31}P shifts for organophosphorus compounds [22], phosphine oxides of the type $Ph_2\overset{\overset{O}{\|}}{P}R$ have ^{31}P shifts in the range δ+21 to δ35 ppm. Phosphinates of the type $Ph_2\overset{\overset{O}{\|}}{P}OR$ have ^{31}P shifts around δ31, and phosphinites have shifts between δ105 and δ115 ppm.

A singlet at δ106 for diphenylmenthylphosphinite (DPMPH) showed that all the starting chlorophosphine had been consumed and the product was almost certainly a phosphinite, which is stable for hours at +25°C. Exposure to air or moisture gave rise to peaks at δ_P 32 and 13 ppm with disappearance of the singlet at 106 ppm.

The [1]H N.M.R. of DPMPH showed no menthol OH in the product, as well as the absence of phosphine oxides. Monitoring the reaction by I.R. revealed the disappearance of the menthol OH stretch and the growth of the P-O-C stretch of the phosphinite at 1017 cm^{-1} [23]. Any contaminating amine salt, detectable by I.R. absorptions at 2495 and 2595 cm^{-1} was easily removed by cyclically dissolving the product in ether, filtering and then removing the solvent. On exposure of the I.R. plates to air; the OH stretch of menthol reappeared, consistent with hydrolysis of the phosphinite to regenerate menthol.

Many phosphinite preparations include a washing of the

product with alcohol, to remove excess amine hydrochloride [17].
Washing the DPMPH with degassed and dried ethanol or methanol
caused the appearance of oxidation products in the [1]H N.M.R.
spectrum. It is unlikely that hydrolysis or oxidation by air
was responsible, as solutions of the phosphinite in
dichloromethane are easily handled using the same precautions
(under nitrogen) without deterioration. Addition of ethanol to
a solution of the phosphinite in dichloromethane at room
temperature showed the appearance of an extra [31]P N.M.R.
resonance at δ110, and eventually a signal at δ35. The [31]P
shift of Ph_2POEt is +109.5 ppm [24], and that of $OPC_2H_5(C_6H_5)_2$
is +35 ppm. This data is consistent with trans-esterification
followed by isomerization, (Scheme 4).

$$Ph_2POMenthyl \ + \ EtOH \ \rightleftharpoons \ Ph_2POEt \ + \ Menthol$$

$$\overset{O}{\underset{\|}{Ph_2PEt}}$$
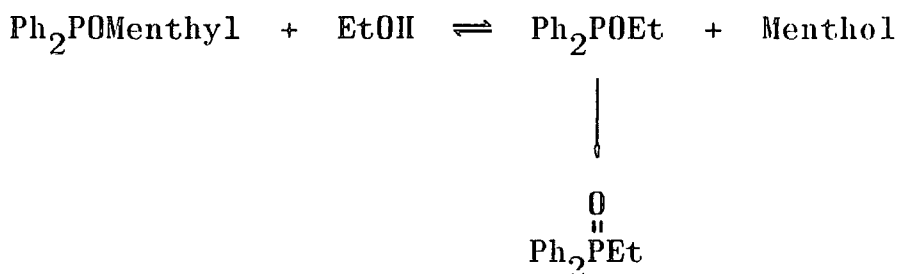
Scheme 4

Attempts were made to further purify the phosphinite.
Bourson et al. distilled their phosphinite (based on DIOP), at
10^{-4} mmHg collecting the product at 240°C, [17]. Heating DPMPH
under high vacuum gave only menthol as the distillate and the
material in the flask began to char above 130°C.
Recrystallization from several solvent systems e.g. pyridine,

pyridine/hexane, dichloromethane/hexane, failed to produce
crystals in all cases. Brunner [21] had claimed to have
purified the phosphinite by low temperature chromatography.
Thin layer chromatograms using both silica and alumina, with a
variety of solvents, showed only one component in the
phosphinite. Thus once the product had been crystallised and
checked for impurities by T.L.C., N.M.R. and I.R. it was used
without further purification. The phosphinite was stable for
many months at -18°C and a ^{31}P spectrum was taken prior to using
any of the material which had been stored.

2.2.2. Preparation of Diphenylneomenthylphosphinite

Initial ^{31}P N.M.R. experiments performed by addition of
Ph$_2$PCl solution to a cooled solution of neomenthol in
tetrahydrofuran showed the formation of a phosphinite at δ+107.
A full-scale preparation, using the same methods as for menthol,
led to the isolation of a viscous oil, the ^{31}P N.M.R. spectrum
of which in THF showed a major peak at δ107, but also smaller
signals at δ31 and δ11. The solution was stored overnight at
-18°C and the ^{31}P spectrum re-run. The phosphinite peak was
greatly diminished. After six hours at room temperature, the
ratios of the peaks at δ107, δ31 and δ11 were 1:4:4. Several
further attempts at the preparation using different solvents and
reagents failed to give a homogeneous product. The oil was
stable for 2-3 days at -18°C but did not crystallize.

2.2.3. The Preparation of 2,2'-Bis(diphenylphosphinoxy)-1,1'-
        binaphthyl

The only reference to the preparation of this phosphinite
is a short communication [5] in which no experimental details

are given. It was stated that the phosphinite was prepared using diethylaminodiphenylphosphine in ether, and was purified by crystallization from ethanol. Another short reference to the preparation of a phosphinite using Et_2NPPh_2 also does not give any experimental detail, [14]. Et_2NPPh_2 was prepared by reacting chlorodiphenylphosphine with diethylamine in ether, [25] the aminophosphine was purified by distillation prior to use. Stirring the phosphine with binaphthol in ether at room temperature gave only a ten percent conversion to the phosphinite, as judged by ^{31}P N.M.R. Refluxing the two reactants overnight in ether did not give more than 30% conversion and oxidation products began to appear. As binaphthol is relatively expensive, experiments were conducted on menthol to try to increase the yield from the generation of phosphinite using diethylaminodiphenylphosphine. Initial ^{31}P N.M.R. experiments showed that mixing stoichiometric quantities of the phosphine and menthol in THF gave around 5% conversion to the phosphinite. Heating a melt of menthol and the phosphine to around 100°C for 5-10 minutes also failed to give high conversion to the phosphinite (followed by ^{1}H N.M.R.). Further experiments were conducted in the presence of triethylamine, and acetic acid in catalytic and stoichiometric amounts, with and without solvent at various temperatures. In no cases was there substantial phosphinite formation, and in many experiments oxidation products formed. Using neomenthol similar results were obtained, therefore an alternative method for preparing 2,2'-bis(diphenylphosphinoxy)-1,1'-binaphthyl was sought. ^{31}P N.M.R. spectra of solutions of chlorodiphenylphosphine and

binapthol in THF in the presence of triethylamine showed efficient phosphinite formation. A stable product was obtained by carrying out the reaction in pyridine with a slight excess of chlorodiphenylphosphine which was removed from the product by washing with hexane.

2.2.4.   The Preparation of 2,3-Bis(diphenylphosphinoxy)butane

Reaction of 2,3-butane diol with two equivalents of chlorodiphenylphosphine showed a phosphinite resonance at $\delta 109$ in its ^{31}P N.M.R. spectrum which was only $\frac{1}{4}$ the intensity of a peak at $\delta+32$; $\frac{1}{2}$ that at δ-16 and δ-35. Variation of solvent, reaction temperature and substitution of Et_2NPPh_2 for Ph_2PCl did not improve the yield of phosphinite. This synthesis was abandoned.

2.3.   (NICKEL AND) PALLADIUM COMPLEXES OF PHOSPHINITES AND PHOSPHINES

The zerovalent palladium complexes of the prepared phosphinites were sought as new hydrocyanation catalysts. The preparation and isolation of some of those complexes are described in this section.

One approach was to reduce the palladium(II) chloride complex of the ligand in the presence of free ligand. This complex was itself obtained from dichlorobisbenzonitrile palladium(II), Scheme 5.

2.3.1.   Diphenylmenthylphosphinite Complexes

The L_2PdCl_2 complex was prepared in 50% yield from $(PhCN)_2PdCl_2$ and L_2 in benzene. Unlike many other L_2PdCl_2 complexes $(DPMPH)_2PdCl_2$ did not precipitate from the reaction

$$PdCl_2 \xrightarrow[\text{PhCN}]{\text{Hot}} (PhCN)_2PdCl_2 \xrightarrow{L_2} L_2PdCl_2$$

$$L_2PdCl_2 \xrightarrow[\text{of } L_2]{\text{Reduction in presence}} L_4Pd$$
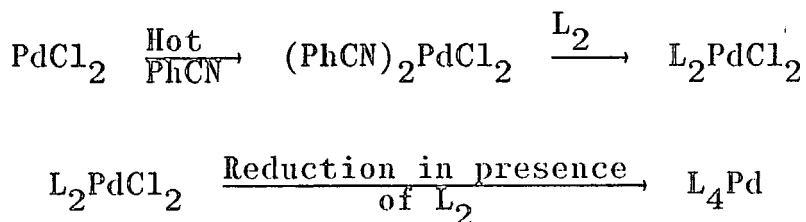
Where L_2 = 2 monodentate or 1 chelating phosphorus(III) compound.

Scheme 5

solution on addition of petroleum ether, therefore the solvent was removed and the complex purified by precipitation from a minimum volume of warm benzene. The use of toluene as the solvent for the reaction gave consistently lower yields.

The ^{31}P N.M.R. spectrum of the complex showed two singlets which were of different intensities depending on sample history. The coordination chemical shift $\Delta\delta$ was -7. The two peaks are probably due to cis/trans isomers of the square planar d^8 palladium(II) complex. Bisbenzonitrile palladium chloride has a cis geometry [26], but cis or trans $PdCl_2L_2$ complexes may be produced when benzonitrile is replaced by L in benzene, the amount of each isomer depending on the ligand [27].

The trans isomer which minimises steric interactions between the phosphinites ought to be more stable, however the major peak in all but one preparation of the complex is the one to lower frequency ($\delta^{31}P$ 98.00), often being less than one fifth

of the intensity of the peak at $\delta 100.0$. The reported ^{31}P resonance of phosphine ligands in trans-L_2PdCl_2 complexes typically occurs 90 - 110 Hz to higher frequency of the cis-L_2PdCl_2 complexes [28]. The sample of (DPMPH)$_2$PdCl$_2$ which did have more of the higher frequency peak had been stored for some time at room temperature, suggesting that isomerization may have occurred. However such assignments must be made with care. For example in the analogous cis and trans-L_2PtCl_2 complexes. the trans complex resonates at lower frequency than the cis, [29].

In view of the low yield of (DPMPH)$_2$PdCl$_2$ relative to that obtained for analogous complexes using other phosphorus ligands, direct reduction of palladium dichloride in dimethylsulphoxide with hydrazine hydrate in the presence of free ligand, [9] was attempted: only decomposition products were obtained from these experiments. The reduction of (DPMPH)$_2$PdCl$_2$ to the zerovalent palladium complex was complicated by the desire to avoid the use of ethanol, and contact with water. Commonly used reduction techniques involve sodium borohydride or hydrazine hydrate in ethanol or water. Attempts to precipitate a complex from the reduction of (DPMPH)$_2$PdCl$_2$ by hydrazine hydrate in ethanol led eventually to the formation of colloidal palladium, although it appeared initially that reaction had occurred. This was supported by ^{31}P N.M.R. experiments. Addition of a solution of DPMPH in dichloromethane to two equivalents of hydrazine hydrate, followed by addition of a solution of (DPMPH)$_2$PdCl$_2$ in dichloromethane resulted in an effervescent exothermic reaction from which gas was liberated for around one minute, and the

solution became orange red. ^{31}P N.M.R. spectra taken after a similar reaction in a cooled N.M.R. tube showed the resonances of (DPMPH)$_2$PdCl$_2$ had gone, and a new resonance at δ115 had replaced it. A trace of free ligand remained at δ106, together with small signals at δ31 and δ20.5 ppm due to decomposition. The resonance at δ115 was attributed to a zerovalent palladium DPMPH complex. The position of the zerovalent complex bound ligand signal is to higher frequency than the free phosphinite, whereas the bound phosphinite of (DPMPH)$_2$PdCl$_2$ resonates to lower frequency of the free phosphinite. This situation occurs with many other phosphorus ligands in nickel and palladium complexes, i.e. the coordination chemical shift $\Delta\delta$ is negative for M(II) complexes and positive for M(0) complexes, e.g. the ^{31}P N.M.R. shifts for Pd[P(OPh)$_3$]$_4$ δ138 ppm, P(OPh)$_3$ δ127 ppm, Cl$_2$Pd[P(OPh)$_3$]$_2$ δ82.6 ppm. This is not necessarily always the case: for DIOP with palladium, both coordination shifts are positive.

Reaction of a dichloromethane solution of (DPMPH)$_2$PdCl$_2$ and DPMPH with an ethanol solution of sodium borohydride on an N.M.R. scale also showed the formation of a major species at δ^{31}P 115 ppm, small peaks at δ21 and δ32 ppm were observed.

The technique finally used to generate the material which was studied involved carrying out the borohydride reduction in a minimum volume of solvent and removing the solvent about ten minutes after the solution had attained an orange colour. The remaining oil was washed briefly with ethanol to remove NaCl, unreacted NaBH$_4$ and DPMPH. This orange oil could be stored at -18°C for months, and on dissolution in dichloromethane, give a

solution with a major peak at $\delta115$ with only small ligand decomposition peaks.

Further support for the fact that a zerovalent complex of DPMPH had indeed been formed came from ^{31}P N.M.R. experiments with bis-dibenzylideneacetone palladium(0). This complex is often used to generate palladium(0) complexes in situ. Addition of four equivalents of DPMPH to a dichloromethane solution of bis-dibenzylidene acetone palladium(0) showed a single peak in the ^{31}P N.M.R. spectrum at $\delta115$, the intense dark violet colour of the Pd(dba)$_2$ complex being quickly discharged to give an orange solution.

2.3.2. <u>2,2'-Bis(diphenylphosphinoxy)-1,1'-binaphthyl Complexes</u>

The insolubility of the phosphinite in ethanol led to difficulties in attempts to prepare palladium complexes of the ligand, so ^{31}P N.M.R. experiments with Pd(dba)$_2$ were conducted.

Addition of two equivalents of the phosphinite to one of Pd(dba)$_2$ led to the phosphinite peak in the ^{31}P N.M.R. spectrum being largely replaced by several peaks, the largest of which were at $\delta145$ and $\delta131$. Smaller peaks, probably due to decomposition products appeared at $\delta38$, $\delta25$, $\delta20$ and δ-23 ppm. After four hours, the free phosphinite peak had disappeared and the $\delta145$ and $\delta131$ peaks ($w_{\frac{1}{2}}$ = 350 Hz) dominated the spectrum. Addition of excess phosphinite produced a sharp free ligand peak at $\delta115$, the $\delta145$ and $\delta131$ ppm peaks were unaffected. The two signals may be caused by exchanging conformations of the chelate ring.

2.3.3. <u>Bis-1,4(diphenylphosphino)butane Complexes</u>

It was intended to use the chelating phosphine

bis-1,4-diphenylphosphinobutane as a model ligand in the study of hydrocyanations, particularly the mechanism; Jackson and co-workers had reported preparing the zerovalent complex of the phosphine [30] but had not characterised it or the intermediate palladium(II) complex.

The complex $[Ph_2P(CH_2)_4PPh_2]PdCl_2$ was isolated for this study by precipitation from benzene following addition of $Ph_2P(CH_2)_4PPh_2$ to $(PhCN)_2PdCl_2$. The complex was conveniently isolated by centrifugation in 40% yield. The fast atom bombardment mass spectrum of the complex showed a collection of peaks with the palladium isotope pattern centred around 567 corresponding to $[LPdCl]^+$. The complex was found to be insoluble in dichloromethane and was subsequently prepared in 85% yield by reaction of dichloromethane solutions of ligand and $(PhCN)_2PdCl_2$. The insolubility of the complex precluded solution N.M.R. characterization. The in situ method for generation of palladium(0) species was clearly more convenient. It was used in preference for testing the ability of various ligand complexes to hydrocyanate a range of substrates.

2.4. HYDROCYANATIONS

Hydrogen cyanide is extremely toxic and must be handled with great care and respect, full details of safety precautions are described in the experimental section (Chapter 5). Reactions requiring the use of HCN were carried out in sealed glass pressure tubes (Carius tubes) by condensing HCN into the tube as the last ingredient before sealing. Due to the small quantities of HCN used, and the greater difficulty in devising a

safe process, a flow system for HCN addition was not used in this study of hydrocyanations.

2.4.1. Alkene Hydrocyanations

As control reactions to test experimental technique. two literature preparations were carried out. The first used preformed palladium(0) tetrakistriphenylphosphite to catalyse the addition of HCN to norbornene at $120^{\circ}C$ giving exo-norbornane carbonitrile. A similar reaction with preformed nickel(0)-tetrakistriphenylphosphite led to the isolation of the product nitrile in 70% yield which compares well with the literature yield of 80%, [9].

Before attempting any asymmetric hydrocyanations, the addition of HCN to some potentially interesting substrates were investigated using $Pd[P(OPh)_3]_4$ and $Ni[P(OPh)_3]_4$. These are efficient catalysts for other alkenes.

2.4.2. Hydrocyanation of Vinyl Acetamide

The addition of HCN to enamides of the type $R_1R_2C=CR_3NHAc$ followed by acidic hydrolysis may give alanine or substituted alanines, (Scheme 6).
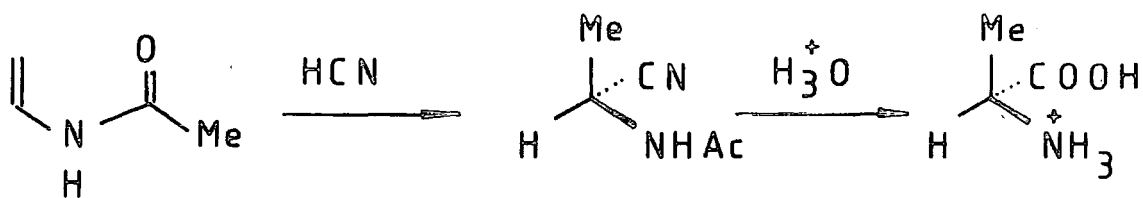
Scheme 6

Vinyl acetamide was prepared from a literature method [34]. (Scheme 7). Two moles of acetamide were condensed with one mole

of acetaldehyde to give ethylidenebisacetamide 9. This was pyrolysed to give vinyl acetamide and acetamide, which were separated by chromatography.

$$2CH_3\overset{\overset{O}{\|}}{C}NH_2 \quad + \quad CH_3CHO \quad \longrightarrow \quad CH_3\overset{\overset{NHCOCH_3}{|}}{\underset{\underset{NHCOCH_3}{|}}{CH}}$$

9
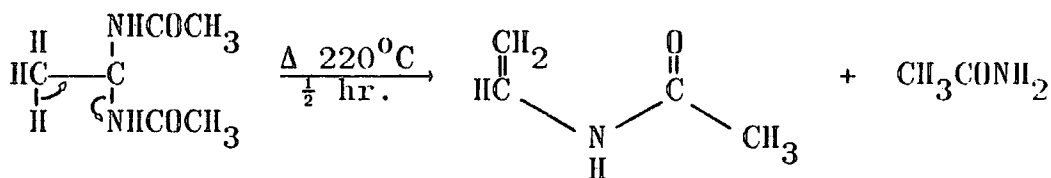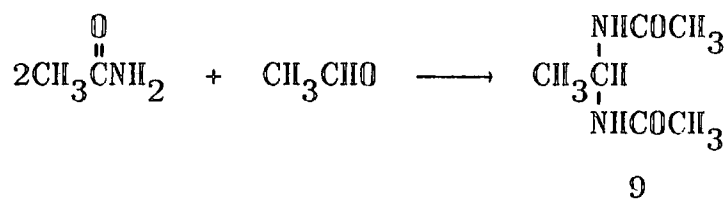
Scheme 7

Experiments carried out using the nickel(0) and palladium(0) tetrakistriphenylphosphite (as well as a control experiment using no catalyst), yielded a brown tarry residue containing more than one component (by [1]H N.M.R. and T.L.C). No simple addition products were detected, nor did any starting material remain. It is likely that polymerisation occurred. The reactions were made difficult by the need to use very small quantities (~ 100 mg) of the enamide due to repeatedly poor yields from the pyrolysis stage. If more material had been available, lowering the reaction temperature from 120°C to around 40°C may have avoided the competing polymerisation.

2.4.3. Hydrocyanation of 1-Tetradecene

Long chain aliphatic compounds with an even number of

carbon atoms are readily available from natural sources. The rarer odd chain length compounds may be formed by anti-Markovnikov addition of HCN to long chain terminal alkenes. These nitriles may be easily converted to cationic surfactants. Analysis of the products from reactions in the presence of Ni(0) and Pd(0) catalyst systems showed no evidence of nitrile formation. It appeared that some double bond isomerization had occurred preferentially as deduced by [1]H N.M.R. analysis of the products.

2.4.4. Hydrocyanation of Vinyl Acetate

Vinyl acetate was chosen for study because

(i)   of its similarity to vinyl acetamide

(ii)   it undergoes base catalysed addition of HCN

(iii)   as with vinyl acetamide there is a possibility that the carbonyl group may coordinate to the metal centre.

A control reaction having all reactants present except the zerovalent metal complex gave no hydrocyanation products. The product nitrile was easily isolated by distillation (b.p. 67 - 70°C, 14 mmHg) and identified by [1]H N.M.R. In all cases where hydrocyanation occurred, the product was exclusively 2-acetyl-oxypropanenitrile 10 none of the 3 isomer was formed.   Table 1

$$CH_3$$

H — C — CN

OAc

10
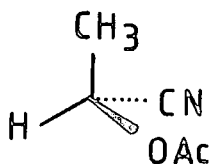
summarises the results of subsequent reactions. In 1985 Tolman reported that vinyl acetate was not hydrocyanated in the presence of $Ni[P(o\text{-}o\text{-}tolyl)_3]_3$ [32]. $Ni[P(OPh)_3]_4$ which is

TABLE 1. Hydrocyanation of vinyl acetate in benzene

Reaction No.	Catalyst	Temperature	Time	Yield of 10
1	None	120^oC	18 hrs.	-
2	$Ni[P(OPh)_3]_4$	120^oC	18 hrs.	85%
3	$Ni[P(OPh)_3]_4$	80^oC	24 hrs.	75%
4	$Pd[P(OPh)_3]_4$	120^oC	18 hrs.	81%
5	$Pd[P(OPh)_3]_4$	80^oC	24 hrs.	83%

obviously similar, catalyses the hydrocyanation to give the nitrile in around 80% yield. The analogous palladium complex also catalyses the addition.

Palladium(0) complexes (generated in situ from $Pd(dba)_2$ or $Pd_2(dba)_3 \cdot C_6H_6$) of the asymmetric ligands DPMPII, 2,2'-bis(diphenylphosphinoxy)-1,1'-binapthyl and DIOP failed to catalyse HCN addition to vinyl acetate. A reaction in the presence of a catalytic amount (1/155 with respect to HCN) of triethylamine using the DIOP ligand produced a 35% yield of the nitrile. Sadly the material was optically inactive. It is almost certain that the nitrile was formed by base catalysed HCN

addition rather than by a metal catalysed route.

2.5. HYDROCYANATION OF NORBORNENE

Norbornene was chosen as a test substrate for asymmetric hydrocyanations because it was the substrate used in the only reported asymmetric hydrocyanation prior to this study. In order to test the validity of using 1,4-diphenylphosphinobutane as a model ligand for later mechanistic studies, the ability of the palladium(0) bis-biphosphine complex to catalyse the addition of HCN to norbornene was tested. Norbornane carbonitrile was isolated in 25% yield (compared to a 15% literature yield).

The nitrile from the above, and all subsequent norbornene hydrocyanations was exclusively exo-norbornane carbonitrile 11: none of the endo-diastereoisomer 12 was detected in any reaction.
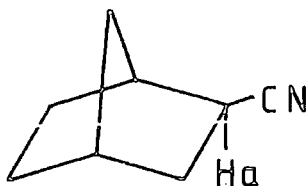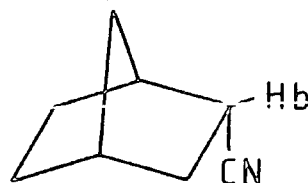
11   12

The assignment of exo-conformation to the nitrile was made by comparison of the product with samples of pure exo isomer and a mixture of exo and endo isomers. [1]H N.M.R. spectra of the two isomers are quite different due to the different shift of an exo versus an endo proton, (H_b vs. H_a) and the change in the coupling to vicinal protons. A G.L.C. analysis was also used to

differentiate between the two isomers.

2.6. ATTEMPTED HYDROCYANATIONS USING PHOSPHINITE LIGANDS

(i) DPMPH. DPMPH was tested first, as its preparation was straightforward to give relatively large quantities of chiral phosphinite. (2 - 5 g of the ligand were required for each hydrocyanation.) Using standard conditions, of 120°C and 18 hours of reaction time, no product carbonitrile was detected during the work-up. Longer reaction times (36 hours) also failed to produce any nitrile. Phosphorus N.M.R. spectra of the reaction solutions taken <u>after</u> opening the Carius tubes showed only phosphorus oxidation products. Neither phosphinite complex nor phosphinite remained. It was thought that the high temperature may have decomposed the complex and ligand, although subsequent experiments conducted whilst trying to purify the phosphinite by distillation showed that the ligand was stable at 120°C for over twenty minutes. Lower temperature hydrocyanations were given longer reaction times and the following combinations were tried:

   (i)   80°C 18 hours;

   (ii)   40°C 36 hours;

   (iii)   Room temperature 96 hours.

In each case, despite careful work-up of each reaction, no trace of norbornane carbonitrile was found. Inspired by the change in the yield from norbornene hydrocyanations simply by increasing the catalyst to substrate ratio, (increasing the ratio from 1:700 to 1:130 increased the yield of norbornane carbonitrile

from 7% to 86%) a final experiment with an increased catalyst to
substrate ratio was conducted. (The ratio was increased from
1:130 to 1:40.) After 18 hours at 80°C this reaction also
failed to give any nitrile product.

(ii) 2,2'-Bis(diphenylphosphinoxy)-1,1'-binapthyl. The ligand
is bidentate, so the catalyst to substrate ratio used initially
was 1:700. No norbornene hydrocyanation was observed at 120°C
for 18 hours using either HCN or acetone cyanohydrin. Lowering
the reaction temperature to 40°C and allowing the reaction to
proceed for 48 hours had no effect, and increasing the catalyst
to substrate ratio to 1:100 was also unsuccessful.

2.7. HYDROCYANATIONS CATALYSED BY BIPHOSPHINE PALLADIUM COMPLEXES

The failure of all the above reactions with phosphinite
ligands and the failure of DIOP to hydrocyanate vinyl acetate
led to a thorough checking of the reactants, particularly the
palladium(0)dba$_2$. In order to be sure that the techniques and
chemicals used were satisfactory, the hydrocyanation of
norbornene using Pd(DIOP)$_2$ (generated in situ from Pd(dba)$_2$) was
undertaken. Norbornane carbonitrile was isolated from the
reaction in 60% yield (with respect to HCN).

2.7.1. Determination of Product Enantiomeric Purity

The optical rotations of resolved samples of the
enantiomers of norbornane carbonitrile have not been determined.
However, the absolute configuration and optical rotations of
resolved samples of the corresponding carboxylic acid have been
measured, [33]. Thus the optical purity of a sample of nitrile

can be determined by measuring the rotation of the acid produced by hydrolysis. If the rotation of the nitrile is also measured before hydrolysis, then the theoretical rotation of pure enantiomers of norbornane carbonitrile can be calculated. This procedure was used by Jackson, giving a value of -12° for $[\alpha_D]^{20}$ of the pure (1S,2S,4R) enantiomer [9], based on $[\alpha_D]^{20}$ of -10.7° for the pure exo carboxylic acid.

The facilities for measurement of optical rotations available initially were very old and relatively inaccurate, therefore independent confirmation of the product enantiomeric purity was carried out by derivatising the acid (obtained by hydrolysis of the nitrile) with (S)methylmandelate under non-racemising conditions to give the diastereomeric esters 13a,b, (Scheme 8). The derivative esters are no longer enantiomers, therefore the [1]H N.M.R. resonances of various protons in the esters are anisochronous, and if sufficiently well separated, the amount of each enantiomer present in the original sample can be determined directly by integration of the separated resonances. The best separation was achieved using d_6-benzene as the solvent for obtaining the spectra.

The esterification was carried out at -10°C in methylene chloride [34]. Dicyclohexylcarbodiimide (DCC) activates the acid to nucleophilic substitution and absorbs the water formed. Dimethylaminopyridine is used as an acyl transfer catalyst.

The reaction procedure was first carried out using a commercial sample of racemic norbornane carbonitrile. The 250 MHz [1]H N.M.R. spectrum of the ester obtained is shown in Figure 1. The mandelate region of the spectrum (from H_a in Scheme 8)

SCHEME 8 DERIVATISATION OF NORBORNANE CARBONITRILE.

1. METHYL MANDÉLATE ESTER.

$\xrightarrow[\text{Pd}L_2]{\text{HCN,PhH}}$

$\xrightarrow{H_3O^+}$

CN

CO_2H

CO_2H

+

$\xrightarrow[\text{DCC}]{\text{DMAP}}$

Ph

HO $\quad CO_2Me$

H

Ph   Ha

Hb   O

CO_2Me

$\underline{13}$

2. N,N DIMETHYLAMIDE DERIVATIVE.

$\xrightarrow[\text{CH}_2\text{Cl}_2]{\text{OH (COCl)}_2}$

$\xrightarrow[\text{H}_2\text{O}]{\text{HNMe}_2}$

Cl

NMe_2
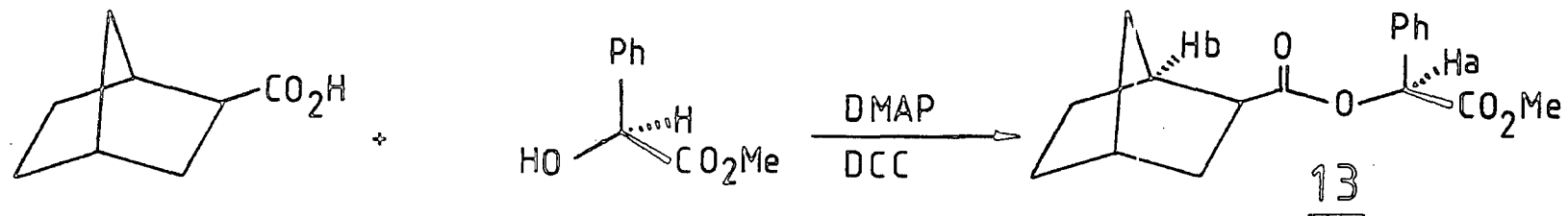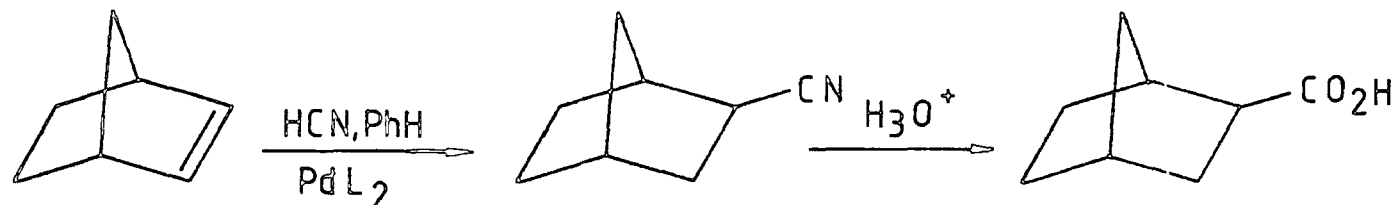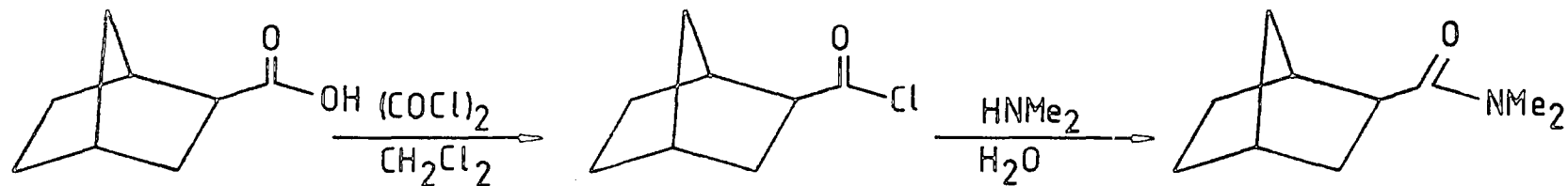
around $\delta5.8$ shows four peaks. The two outer peaks are separated by 0.1 ppm (i.e. $\Delta\delta = 0.1$ ppm) and they integrate 1:1 to each other. The inner peaks have $\Delta\delta$ of only 0.01 ppm. Figure 2 shows an expansion of this region of the spectrum, where it can be seen that the inner peaks also have the same integral as each other. This behaviour is consistent with the presence of both exo and endo nitrile in the commercial sample.

The inner peaks were due to the exo-derivative. This was confirmed by comparison of the relevant spectrum with G.L.C. data. The outer peaks had a higher integral than the inner ones, i.e. they represented the more abundant isomer in the sample. G.L.C. analysis showed that the commercial sample contained two components; present in the same ratio as the [1]H N.M.R. integrals. Addition of the product nitrile from a hydrocyanation reaction increased only the smaller of the peaks.

This analysis was confirmed when some of the nitrile from the hydrocyanation of norbornene catalysed by $Pd(DIOP)_2$ was hydrolysed and derivatized with (S)methylmandelate. The 250 MHz [1]H N.M.R. spectrum of the ester is shown in Figure 3. Preliminary measurements focussed on trying to resolve the peaks at $\delta6.1$. The best spectra (Figure 4) were analysed using a DuPont curve resolver, and also a computer program for measuring the areas of shapes traced onto a pressure sensitive pad. Re-examination of the full proton spectrum showed the alkyl region to be considerably simplified by the removal of the endo isomers (compare Figure 1 with Figure 3). Measurement of the integral of the region led to the conclusion that the peaks at $\delta2.87$ and $\delta2.54$ may be assigned to protons in the esters derived

Figure 1. PROTON NMR SPECTRUM OF METHYL MANDELATE ESTER OF RACEMIC EXO & ENDO NORBORNANE CARBOXYLIC ACID.
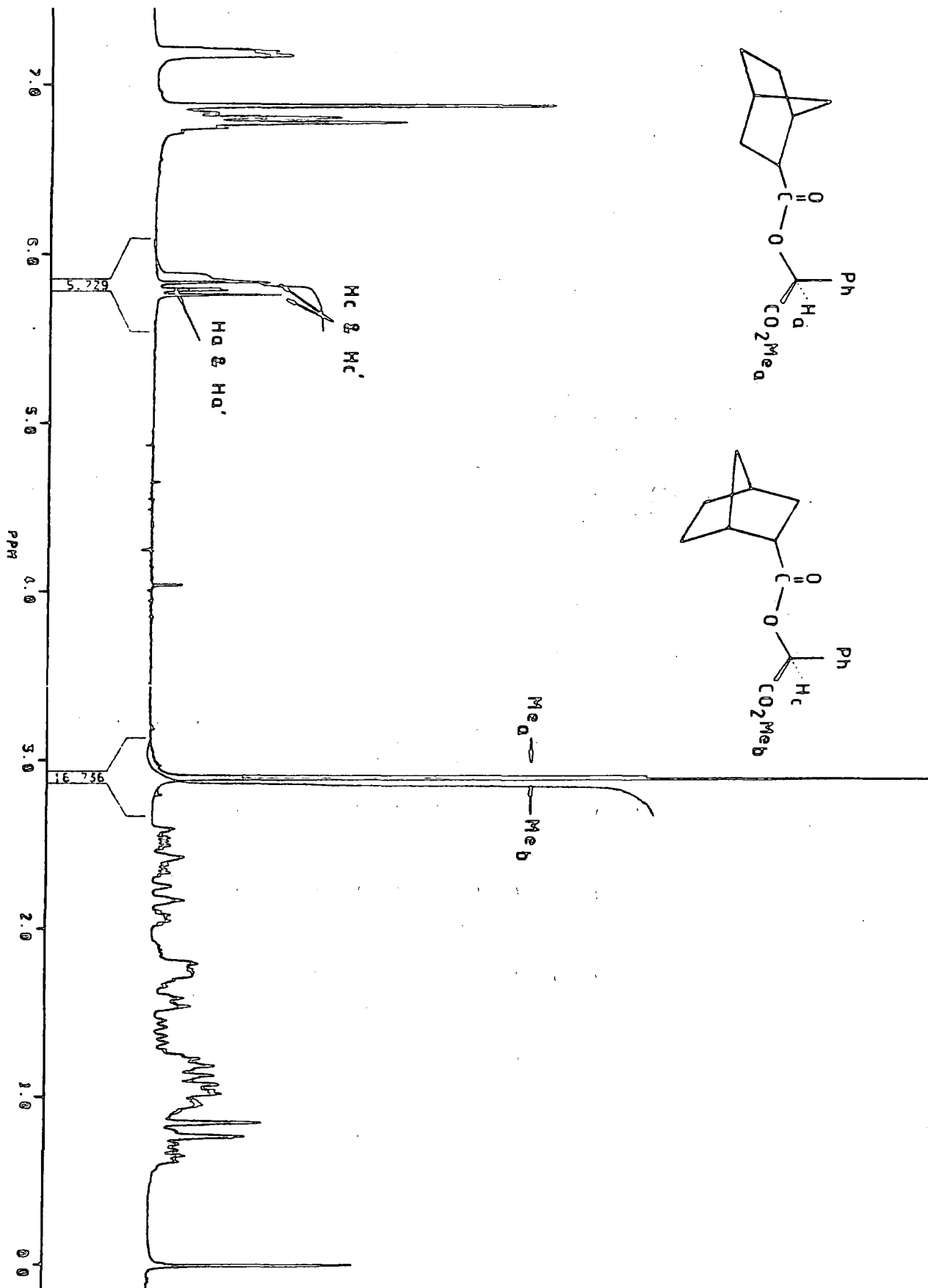
Figure 2. Mandelate Region of Figure 1.

Hc & Hc'

Ha & Ha'
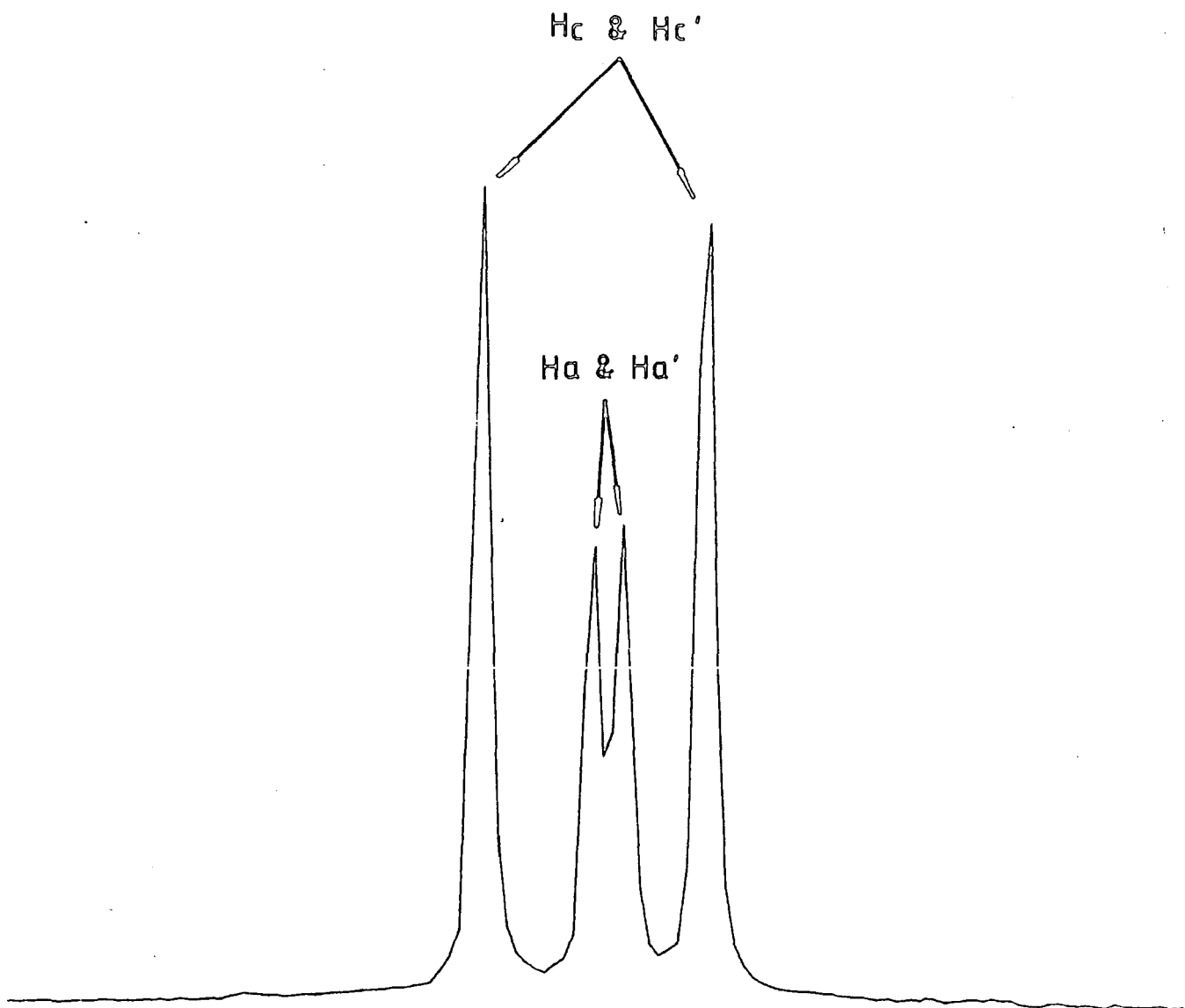
Figure 3. Mandelate Ester of Chiral exo-Norbornane Carboxylic Acid.

Ha & Ha'

Me

Hb & Hb'
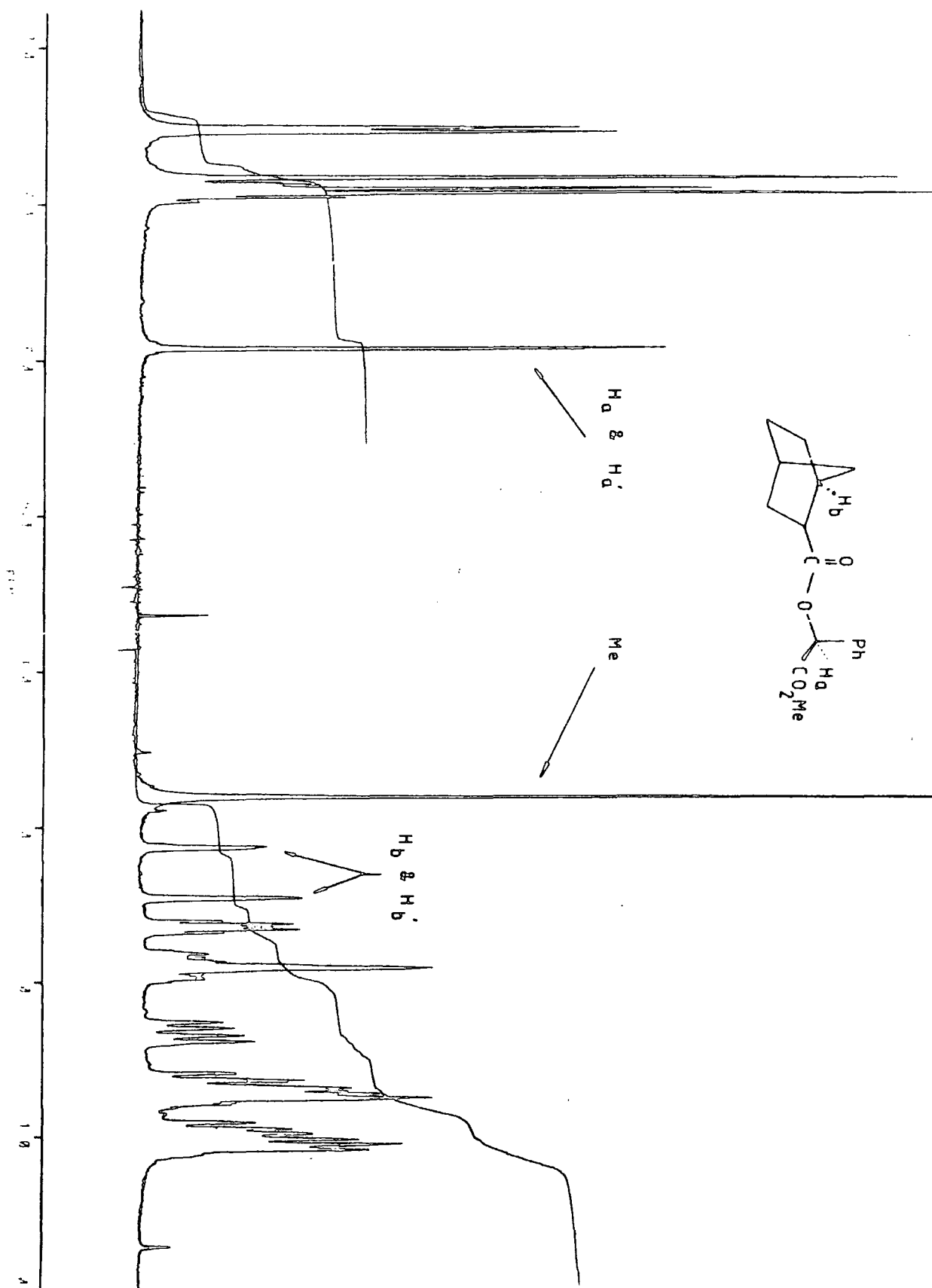
Figure 4. Mandelate Region of Figure 3 ($\sim$6·1ppm)
Expanded for use with Curve Resolver.

Ha & Ha'
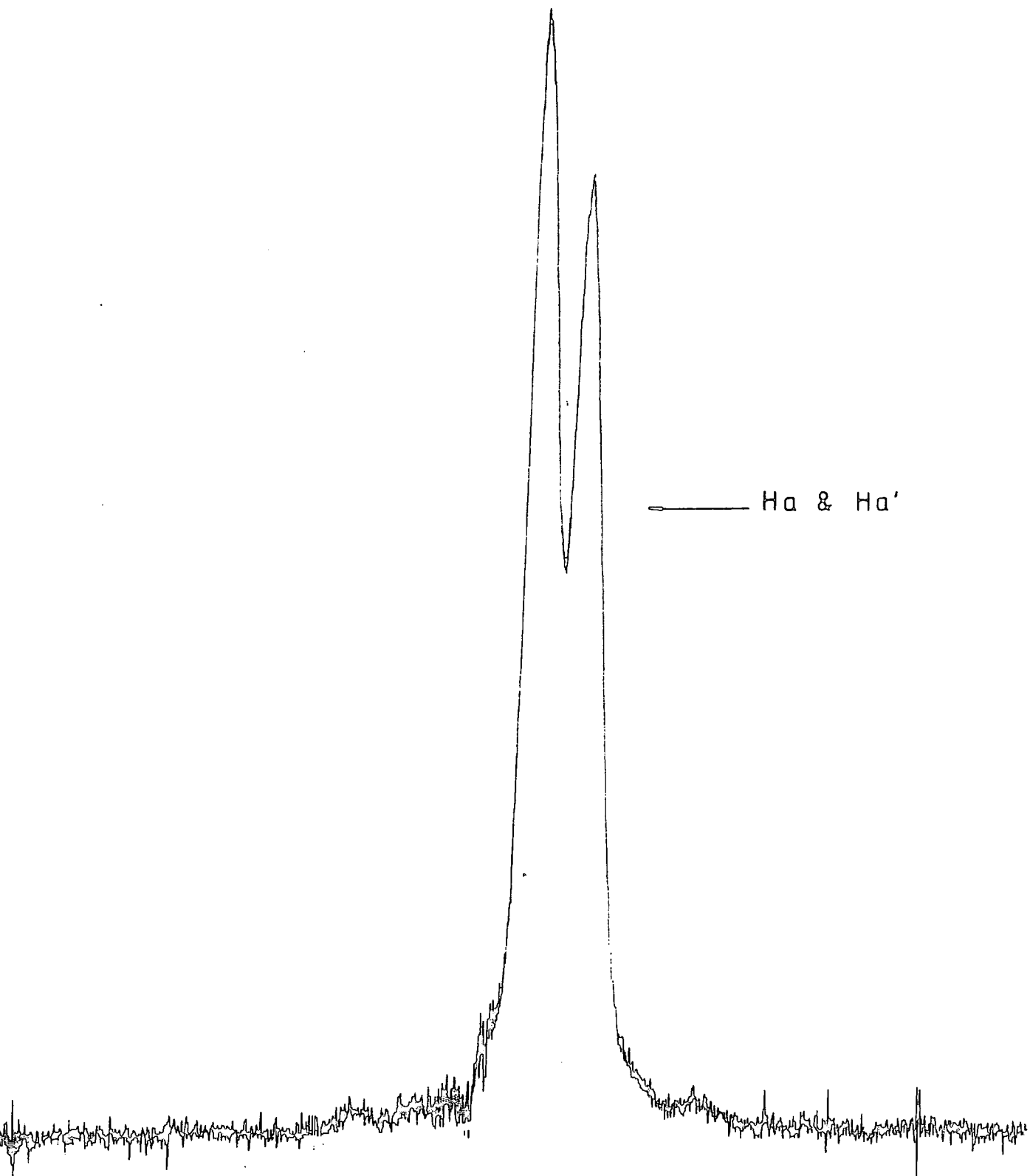
from different enantiomers. The chemical shift, and small
coupling indicates that the resonances are from the bridgehead
norbornyl protons II_b in <u>13a,b</u> [35]. The much greater separation
of these resonances despite their greater distance from the
chiral centre, makes them a more reliable measure of the
relative amounts of each ester present. With $\Delta\delta$ of 0.33 ppm the
peak areas were determined by electronic integration; computer
with pressure sensitive pad, and finally by cutting the peaks
out of the spectrum and weighing the pieces of paper produced.
All of the above methods for both mandelate and bridgehead
protons gave results in close agreement with each other. The
value for enantiomeric excess obtained from the N.M.R. data for
the $Pd(DIOP)_2$ catalysed hydrocyanation of norbornene was 9 ± 1%
enantiomeric excess, the crude optical measurements had
suggested an enantiomeric excess of 17 ± 6%. The optical data
was checked using a highly accurate modern polarimeter
(University of Newcastle-upon-Tyne) to measure the rotation of
both the nitrile and the carboxylic acid from the $Pd(DIOP)_2$
catalysed reaction. The results obtained from these experiments
put the value for enantiomeric excess at 23 ± 1%.

In an attempt to resolve the disagreement, the
N,N-dimethylamide derivative of norbornane carboxylic acid was
prepared (<u>Scheme 8</u>(ii)). In the hope that gradual addition of a
chiral shift reagent, tris-[3-(heptafluoropropylhydroxy-
methylene)-d-camphoratato]europium(III) derivative $(Eu(hfc)_3)$,
would separate the resonances of the methyl groups attached to
the nitrogen for each enantiomer. The resonances of the NMe_2
group were shifted to higher frequency by addition of the shift

reagent, but were not separated well enough before they were too broad to be of use.

Another sample of chiral nitrile was obtained from a hydrocyanation of norbornene catalysed by palladium(0) $BPPM_2$ (vide infra). This sample was hydrolysed and derivatised with (S)methylmandelate. Again the optical data and [1]H N.M.R. data disagreed. The enantiomeric purity as deduced from the N.M.R. data was considerably lower than that obtained from the optical data. The fact that the values obtained from both methods were in a constant ratio for both samples, suggested the possibility that the literature value for the rotation of the exo-norbornane carboxylic acid was wrong. Although this appeared an unlikely cause for the discrepancy, the original reference relating to the rotation of the carboxylic acid was sought.

When the correct reference was finally found [33] it contained a scheme with the value of $[\alpha_D]^{20} = -10.7^0$ next to exo-norbornane carboxylic acid. However the caption to the scheme indicated that this was a measurement made on carboxylic acid derived from a partially resolved sample of starting material. The correct value for the rotation of pure (1S,2S,4R) exo-norbornane carboxylic acid calculated from the partially resolved material is $[\alpha_D]^{20} = -27.8^0$, and this value appeared in a table in the publication. All the optical yields had therefore to be reduced by multiplying by a factor of 0.38. With this correction, the calculated value for pure (1S,2S,4R)-exo-norbornane carbonitrile is -31.5^0, using this value, the proton N.M.R. data and chiroptical data agreed exactly. The claimed optical yields for $Pd(DIOP)_2$ were thus

shown to be 2.6 times lower than originally thought.

2.6.2.   The Use of (2S,4S)-N-(tert-Butoxycarbonyl)-4-
         (diphenylphosphino)-2-[(diphenylphosphino)methyl]-
         pyrrolidine (BPPM)

The failure of the phosphinite ligands, together with the
demonstration of the validity of the techniques used following
the success of the Pd DIOP$_2$ catalysed hydrocyanation led to a
consideration of other chiral chelating phosphines for
assessment in alkene hydrocyanation. One such ligand is BPPM
14.

Ph$_2$P

PPh$_2$

N

C=O

^{t}BuO
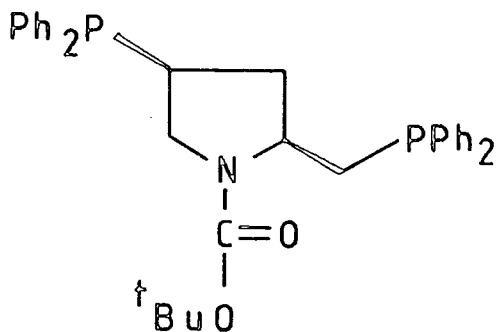
14

A small sample of the ligand, barely sufficient for one
hydrocyanation reaction was obtained from Achiwa in Japan. Due
to the small amount of ligand available; the catalyst to
substrate ratio was reduced from 1:700 to 1:1200. The catalyst
was generated in situ from palladium(0) bisdibenzylidene
acetone. The norbornane carbonitrile obtained from the reaction
had an enantiomeric purity of 20% (by both optical methods and
[1]H N.M.R. determination as described earlier). The chemical
yield was better than that obtained from the Pd DIOP$_2$ catalysed

reaction under identical conditions. It was decided therefore to continue mechanistic and synthetic studies with this promising ligand, synthesizing it, by an adaption of literature procedures, from ℓ-hydroxyproline.

2.7.3. Synthesis of BPPM

The synthesis of BPPM from ℓ-hydroxyproline 15 involves five steps, shown in Scheme 9. In the first step, the acid is esterified to facilitate reduction of the carbonyl to an alcohol. The ester 16 is N-protected by the introduction of a tertiary butoxycarbonyl group to give 17, which is reduced to the diol 18. This material is tosylated to give 19. The final stage involved the displacement of the tosyl groups with diphenylphosphide to give BPPM.

Two similar descriptions of the preparation appear in the literature [36,37]. The methods used in this study represent an improved preparation and are described below.

The ethyl ester was prepared by refluxing ℓ-hydroxyproline in ethanol, dry HCl was generated in situ by addition of acetylchloride.

The next step involved the use of t-butoxycarbonyl azide (BOC azide) 20. This material is explosive and is therefore not commercially available, and it is recommended that alternative reagents are used to introduce the BOC group [38]. The disadvantage of other reagents is their high cost relative to BOC azide, which is prepared, when needed, by treating t-butylcarbazate with nitrous acid, Scheme 10 [39].

SCHEME 9.   SYNTHESIS OF BPPM.

$$NH_2NHCO_2C(CH_3)_3 \xrightarrow{\text{HONO}} N_3CO_2C(CH_3)_3$$

<u>20</u>
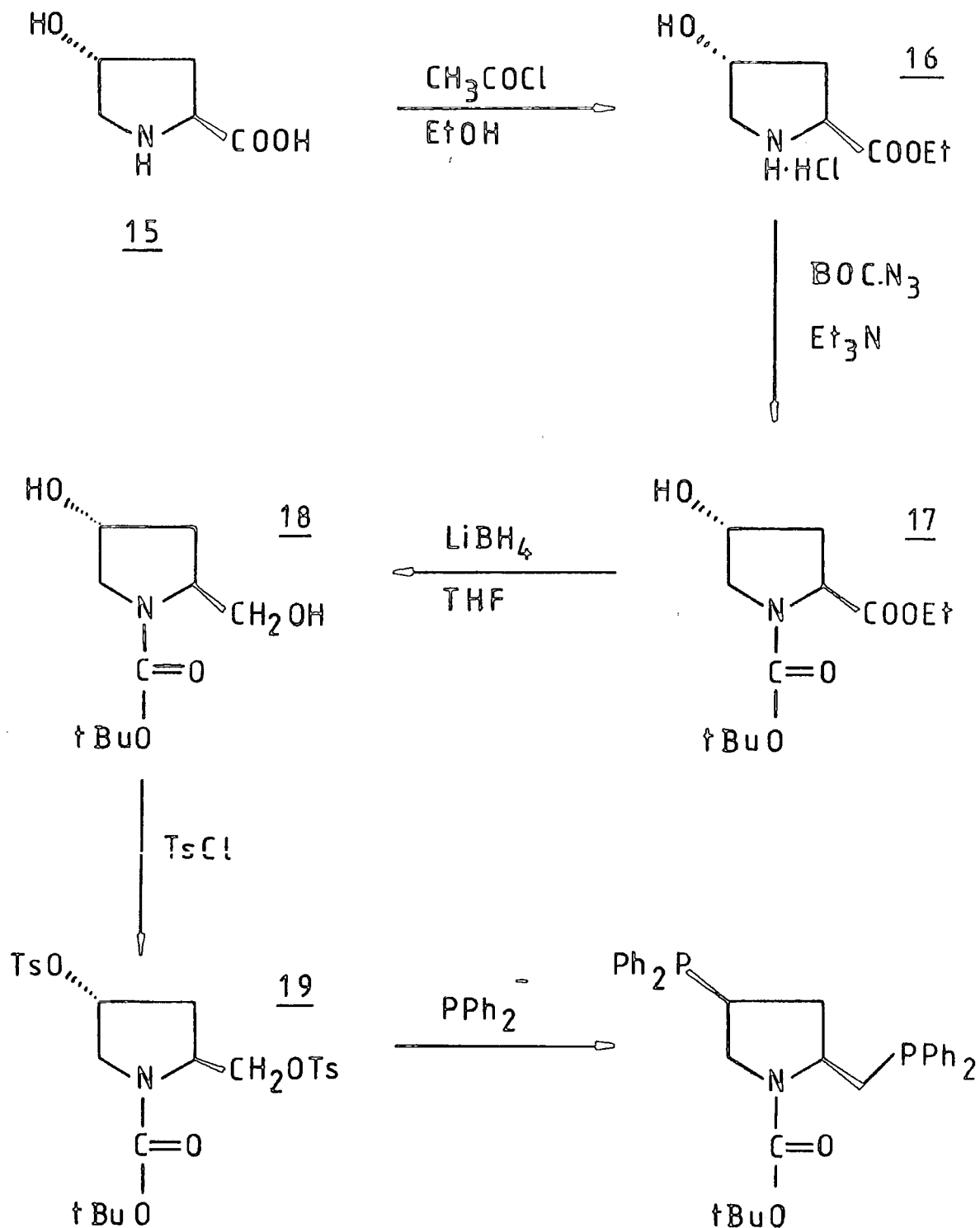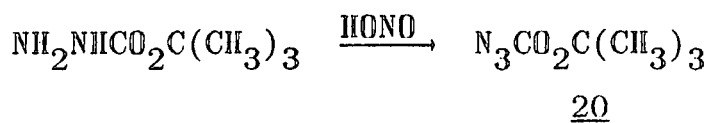
Scheme 10

The synthetic utility of two alternative reagents was therefore investigated. These were (i) di-t-butyldicarbonate (BOC carbonate) <u>21</u> and (ii) 2-t-butoxycarbonyloxyimino-2-phenylacetonitrile <u>22</u>.

(i) <u>The use of di-t-butyldicarbonate</u>. The method was adapted from that of Grieco and co-workers [40], in which the N group of the ester is protected by reaction with BOC carbonate using dimethylaminopyridine (<u>Scheme 11</u>).
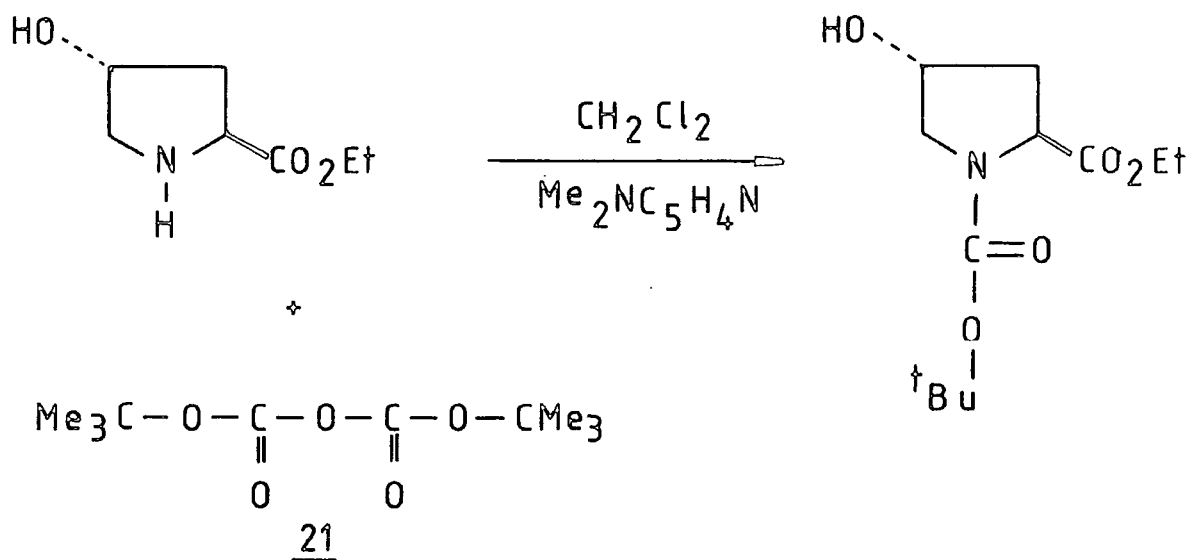
Scheme 11

An initial small scale reaction was violently exothermic, therefore subsequent reactions were cooled until addition of the reagents was complete. Isolating the product by chromatography or distillation proved difficult and impractical. Pure product

was obtained by removing the solvent, then washing the solids
from the reaction mixture with dilute acid to remove the
pyridine. Remaining solid was taken up into hexane, filtered
and washed successively with more acid, saturated aqueous
bicarbonate and finally water. The product was isolated as a
colourless oil in 80% yield.

(ii) The use of 2-t-butoxycarbonyloxyimino-2-phenylacetonitrile
(BOC PhCN). The method used was largely based on that used by
Itoh and co-workers [41]. The procedure involves simply mixing
the reactants and stirring under nitrogen (Scheme 12).
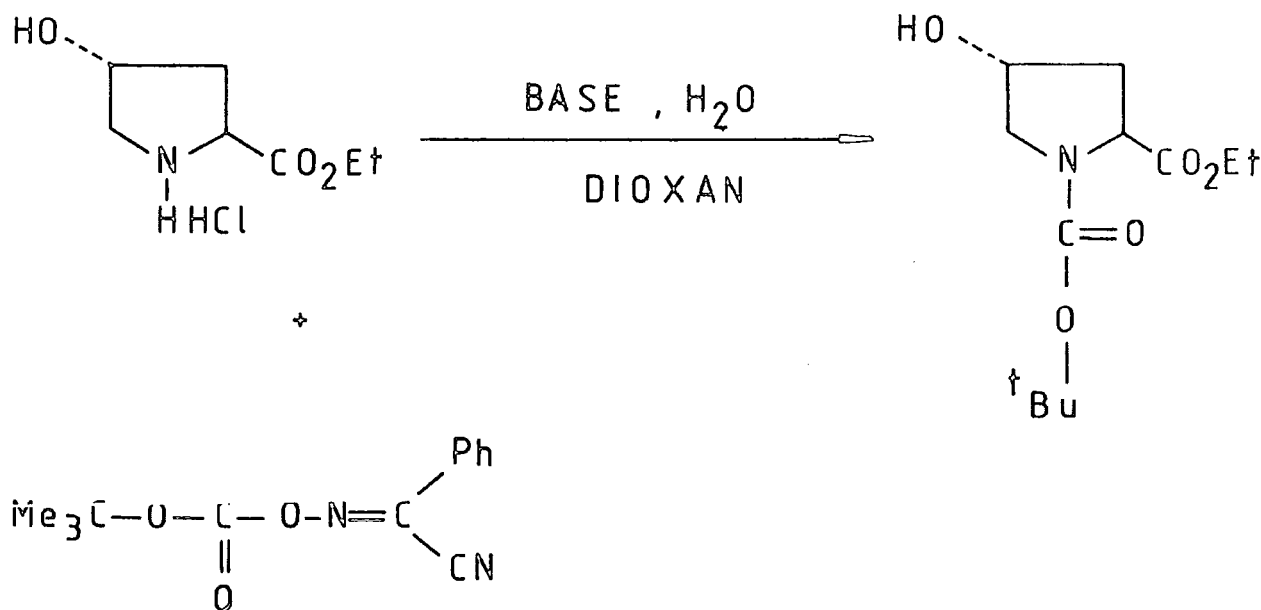
Scheme 12

The critical problem was the removal of oxime formed as a
side-product. Once again distillation and chromatography did
not provide the answer. The oxime was found to transfer to the
aqueous phase only on treatment with dilute NaOH [41]. This
extraction provided a simple means for removal of the oxime,
which could be detected by the resonances in the phenyl region

of the [1]H N.M.R. spectrum. This method yielded the BOC
protected derivative in 95% yield as a pale yellow oil.

(iii) The use of t-butoxycarbonyl azide. The N-protection was
finally carried out on a large scale using the traditional
t-butoxycarbonyl azide. The reagent was prepared by the
literature method [39] as in Scheme 10, although it was used
without purification by distillation. (This practice is
recommended to minimise the risk of explosion.) The reaction
was carried out by heating the amine in a dioxan/water mixture
to 50°C for 15 hours. The product was obtained as a pale yellow
oil in 74% yield by ether extraction.

(iv) Summary of reagents used for BOC protecting of the N group
in 16. Comparing the synthetic utility of the three reagents,
BOC PhCN reagent is the most useful, being both easy to use and
highly reactive, it is however considerably more expensive than
the other two reagents. BOC carbonate is used as a two-fold
excess, which renders it around three times more expensive than
the azide reagent. The use of the carbonate also suffers from
the drawback of requiring stoichiometric amounts of highly
poisonous dimethylaminopyridine. Finally the azide, as already
mentioned, is explosive and several warnings as to its use
appear in the literature. The preparation and subsequent use of
the azide are however quite simple and the starting material is
inexpensive.

The reduction of the protected ester to the dialcohol, and
the subsequent tosylation were carried out according to the
literature preparation [36].

The last stage, that of introducing the diphenylphosphine

groups was carried out using sodium/potassium alloy to cleave triphenylphosphine [42] producing diphenylphosphide anions which readily displace the tosyl groups in an S_N2 reaction to give the chelating diphenylphosphine BPPM. The above technique obviates the use of pyrophoric diphenylphosphine which is reacted in liquid ammonia in the literature procedure. The BPPM oil produced at the end of the preparation is very difficult to crystallize. The best method involves slow crystallization from ethanol (4^0C, 2 days min.).

2.7.4. Hydrocyanation Reactions Catalysed by BPPM Complexes

The first hydrocyanation reaction with palladium(0) $BPPM_2$ using BPPM from Japan gave a comparable chemical yield, but the product had double the enantiomeric purity, of the palladium(0) $DIOP_2$ catalysed reaction.

An increase in the reaction temperature generally leads to a decrease in stereoselectivity. This is found to be the case for most asymmetric hydrogenations [43]. Exceptions involve different mechanisms operating at different temperatures [37]. In the $Pd(DIOP)_2$ catalysed hydrocyanation of norbornene, the optical yield was reported to decrease from 13% at 35^0C to 9% at 120^0C [9] (using corrected optical data). The chemical yield dropped sharply below 80^0C from 92% at 80^0C to 6% at 35^0C.

The temperature dependence of $Pd(BPPM)_2$ catalysed system was found to be similar. Reactions at 40^0C, 80^0C and 120^0C were carried out using BPPM. Chemical yields at 80 and 120^0C were the same. The optical yield decreased from 25% at 80^0C to 20% at 120^0C. No product was isolated at 40^0C, despite an extended reaction time of four days.

The preformed complex $Pd(BPPM)_2$ was prepared in an

analogous manner to Pd(DIOP)$_2$ (Scheme 5). The reduction of the intermediate dichloropalladium(II) complex was carried out by sodium borohydride in acetone/water in the presence of BPPM.

The corresponding nickel complex Ni(0) (BPPM)$_2$ was also prepared, by direct reduction of nickel(II) nitrate or chloride in ethanol using sodium borohydride in the presence of two equivalents of BPPM.

Hydrocyanations were carried out using the preformed palladium and nickel catalysts. Free ligand and substrate to catalyst ratios were maintained at the values used for in situ generation of catalyst. The preformed palladium complex catalysed the addition of HCN to norbornene as efficiently as the catalyst generated in situ; i.e. the active catalyst is the same in both cases, whether the palladium is added as preformed Pd(BPPM)$_2$ or generated in situ from Pd$_2$dba$_3$.C$_6$H$_6$.

The zerovalent nickel complex Ni(DIOP)$_2$ catalyses the addition of HCN to norbornene to give exo-norbornane carbonitrile which is enriched in the opposite enantiomer to that obtained with the corresponding palladium catalyst [9]. This result is remarkable, as it was found that using norbornadiene or 1,4-dihydro-1,4-methanonapthalene 23 as

23
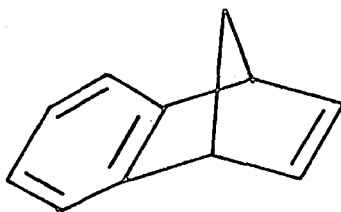
substrates, the nickel and palladium DIOP system gave mono-nitriles which were enriched in the same enantiomer, i.e. the changeover in the sign of rotation of the product on substituting nickel for palladium was only observed when norbornene was the substrate, [9].

The nickel complex of BPPM was tested as a catalyst and was found to give both a low chemical (7%) and optical (4%) yield. The product nitrile was enriched in the same enantiomer as the corresponding palladium complex.

Finally a hydrocyanation of norbornene catalysed by $Pd(BPPM)_2$, using acetone cyanohydrin in refluxing toluene as the source of HCN, gave _exo_-norbornane carbonitrile in the same chemical and optical yield as using HCN.

2.6.5. <u>Hydrocyanations Using 2,2'-Bis(diphenylphosphino)-1,1'-binapthyl, (BINAP)</u>

Binap <u>24</u> is an example of a chelating biphosphine ligand which has shown promise in asymmetric hydrogenations [6,7,8].
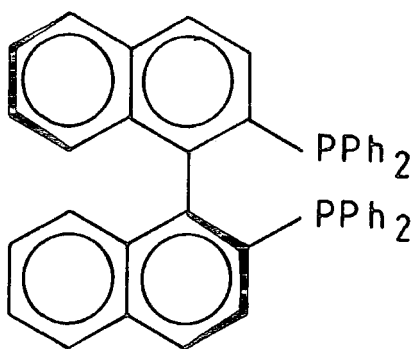
<u>2 4</u>

It is commercially available, but is extremely expensive,
500 mg were purchased in order to undertake preliminary
synthetic and mechanistic studies. Hydrocyanation reactions of
norbornene were carried out at 80°C and 120°C using catalyst
generated in situ from $Pd_2dba_3 \cdot C_6H_6$. The chemical yields were
low, (6%) but the optical yield of 40% is the highest known for
an asymmetric hydrocyanation reaction. The results of
asymmetric hydrocyanation reactions undertaken are summarised in
Table 2. At a reaction temperature of 80°C the optical yield
appears as 34%, which is less than the 40% obtained at 120°C.
The reaction at 80°C was performed on a smaller scale, and due
to the low chemical yield only 38 mg of product nitrile was
obtained. Although the I.R. and [1]H N.M.R. indicated that the

TABLE 2. ML_2 catalysed hydrocyanation of norbornene in benzene

ML_2 Catalyst	Reaction Temperature 0°C	Yield of nitrile (%)	Enantiomeric Purity (± 1%)
Pd(R-DIOP)$_2$	120	60	10R
Pd(S-DIOP)$_2$	80	94	13S
Pd(SS-BPPM)$_2$	120	68	20R
Pd(R-BINAP)$_2$	120	6	40R
Pd(R-BINAP)$_2$	80	6	34R
Pd(R-DIOP)$_2$	120	86	9R
Pd(SS-BPPM)$_2$	80	13	25R
Ni(SS-BPPM)$_2$	120	17	4R

[a] In tetrahydrofuran as solvent.

[b] Refers to the purity of the (1R,2R,4S)-exo-2-cyanonorbornane.

material was almost pure, the melting point was low. The lower value of optical rotation may be partly due to impurities in the sample. Even if this is the case, the margin of error is sufficiently large to say that either the optical yield decreases with decreasing temperature, or that the temperature dependence of the reaction is small.

2.7.6. Other Aspects of the Hydrocyanation Reaction

(i) Solvent. The polarity of the reaction medium can alter the course of a reaction by changing the stability of intermediate species and the rate of their reaction. A more polar solvent favours ionic intermediates. While such effects are observed in asymmetric hydrogenations [44], no change in optical or chemical yield of norbornane carbonitrile was observed when the asymmetric hydrocyanation catalysed by palladium(0) $(DIOP)_2$ was carried out in THF instead of benzene.

(ii) Lewis acid. The effects of Lewis acid added to hydrocyanation reactions were discussed in the introduction. Jackson [9] found that addition of zinc chloride to the $Pd(DIOP)_2$ catalysed reaction of hydrogen cyanide with norbornene did not alter the chemical yield, or the enantiomeric enrichment of the product. The changes in product distribution brought about by Lewis acids in nickel catalysed hydrocyanations vary dramatically with both Lewis acid and substrate [45]. It was considered worthwhile to investigate the influence of at least one other Lewis acid on the reaction. Triphenylboron was chosen because Tolman discovered that it alone brought about large changes in the selectivity of HCN addition to styrene catalysed by nickel complexes [45]. This was thought to be due to its

very large steric bulk relative to other Lewis acids. In Tolman's nickel catalysed reactions, the ratio of acid to metal to HCN was 1:1:4. The triphenylboron complexed preferentially to the cyano ligand bound to nickel. The reaction was greatly slowed by addition of triphenylboron.

Triphenylboron was added to a Pd(0) $DIOP_2$ catalysed reaction of HCN with norbornene. The acid to metal to HCN ratio was a compromise at 2:1:32 and the reaction time was increased to 42 hours. The nitrile formed was exo-norbornane carbonitrile. The chemical yield dropped to 38%: however the enantiomeric purity of the product was unchanged.

(iii) Olefin binding. This topic will be discussed more fully in Chapter 3. The stereochemistry of the binding of the olefin substrate to the metal catalyst is a key factor in asymmetric hydrogenations, indeed high stereoselectivity can be obtained by achiral metal complexes with substrates possessing an asymmetric centre [46]. Successful asymmetric hydrogenations usually require a substrate containing an enamide group, or a closely related structure which is capable of coordinating to the metal both via the olefin bond and the amide carbonyl to give a chelated intermediate, [47]. This fact was an underlying reason for the attempts to catalyse the addition of HCN to vinyl acetate and vinyl acetamide mentioned earlier. In hydrogenation reactions it is well established that alteration of the stereochemistry around a double bond can cause large changes in stereoselectivity, [48]. It was thus decided to examine the hydrocyanation of a pair of E,Z isomers.

First alkenes of the type 25a and 25b were chosen.

$\underline{25\,a}$
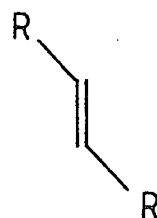
$\underline{25\,b}$

The symmetry of the two alkenes is different, the Z isomer $\underline{25a}$ is C_2 symmetric with a mirror plane. $\underline{25b}$ is C_2 symmetric in a different plane to $\underline{25a}$ and has a centre of symmetry. The two faces of $\underline{25a}$ are both re-si and are indistinguishable, whereas $\underline{25b}$ has a si-si face and a re-re face. Addition of HCN to either olefin would give the same chemical product in each case, thus observation of the enantiomeric purity of the products from the reactions with each olefin would give information as to the importance of olefin binding during the course of the reaction or the lack of it.

E and Z 2-Butenes are gases so the first olefin studied was $\underline{E}$-3-hexene ($\underline{25b}$ with R = Et), using the $Pd(DIOP)_2$ catalyst system. Unfortunately no hydrocyanation products were observed, which is disappointing, as it is reported that the system catalyses the addition of HCN to 3,3-dimethylbut-1-ene, [49]. Similarly neither $\underline{E}$ nor $\underline{Z}$ stilbene (R = Ph) underwent hydrocyanation.

The final pair of $\underline{E}$, $\underline{Z}$ isomers studied were that of crotonitrile $\underline{26a,b}$: no hydrocyanation products were observed.

Me$\diagdown$

CN$\diagup$

<u>26a</u>

Me$\diagdown$

$\diagdown$CN
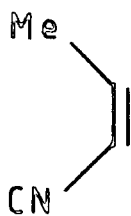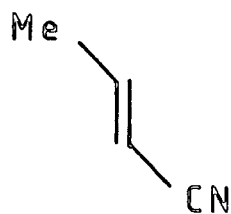
<u>26b</u>

(iv) <u>Platinum catalysis</u>. The complex $Pt(0)(DIOP)_2$ does not catalyse the addition of HCN to norbornene [9]. It was shown during the course of this study that both $Pt(DIOP)_2$ and $Pd(DIOP)_2$ are inert to HCN at ambient temperatures and pressures, (Chapter 3). However the ethene complex Pt DIOP ethene was shown to react with HCN (Chapter 3). It has also been shown that other alkenes readily displace the coordinated ethene from the complex [50]. Platinum DIOP ethene was tested as a catalyst for the hydrocyanation of norbornene under standard conditions. No hydrocyanation products were observed. and the reaction mixture was no longer homogeneous, as a white precipitate had formed. This precipitate was similar to those formed during the course of N.M.R. experiments and is thought to be $Pt(CN)_2$.

(v) <u>Asymmetric cyanohydrin synthesis</u>. The asymmetric addition of HCN to aldehydes to give cyanohydrins has been reported, [51]. Inoue and co-workers used cyclic dipeptide to catalyse the addition. Optical yields were as high as 90% e.e. during the early stages of the reaction, but the product was found to racemize under the reaction conditions. The optical purity of a sample of the cyanohydrin was reduced from 90% to 35% when it was kept at $35^{\circ}C$ for $3\frac{1}{2}$ hours with benzaldehyde and the

catalyst, [52].

A trial experiment using palladium(0) DPMPII to catalyse the addition of HCN to benzaldehyde gave a 38% yield of mandelonitrile after 2 hours reaction time at 35^{0}C in benzene. The reaction was followed by the decrease in the absorption band at 2735 cm^{-1} (ν_{C-H} of benzaldehyde) in the I.R. spectrum. After removal of the solvent the residue was purified by column chromatography to give a mixture of mandelonitrile and unreacted benzaldehyde. The fraction of mandelonitrile in the product was determined by the relative integrals of the peaks due to CHOH of mandelonitrile and the aldehyde proton of benzaldehyde in the ^{1}H N.M.R. spectrum. The optical purity was determined after hydrolysis of the nitrile to give mandelic acid which has a higher specific optical rotation (Scheme 13).
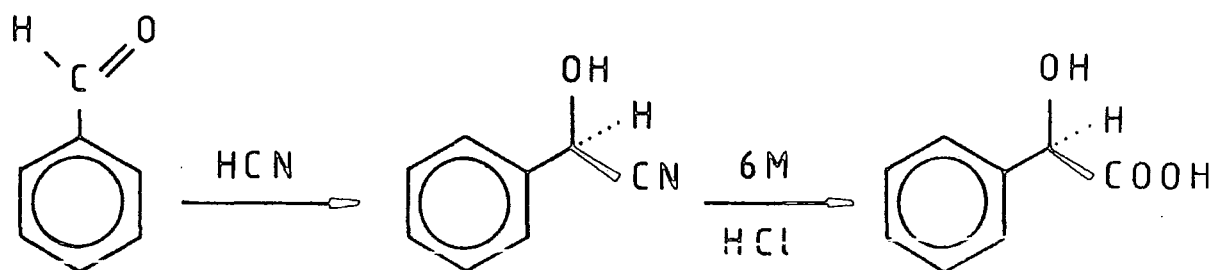
Scheme 13

The product from the reaction was found to have an optical rotation corresponding to 4% optical purity of the nitrile. Further experiments using shorter reaction times or lower temperatures gave low conversion of the aldehyde to mandelonitrile. Attempts to accelerate the conversion by addition of triethylamine to the system resulted in high yields of mandelonitrile, which however showed no optical activity. The results are summarised in Table 3. Attempts to add HCN to

TABLE 3. Reactions of benzaldehyde with HCN in Benzene

Reaction No.	Temperature	Reaction Time hrs.	Added Base	Conversion to Mandelonitrile	Optical Purity
1	35°C	1	-	< 5%	-
2	35°C	2	-	38%	4%
3	25°C	5	-	< 5%	-
4	35°C	1	Et$_3$N	80%	-
5	35°C	2	Et$_3$N	90%	-

acetophenone were unsuccessful, even after prolonged reaction times.

2.8. CONCLUSIONS

Asymmetric hydrocyanation reactions are more severely limited in scope than the related hydrogenations. The range of

substrates appears limited to strained alkenes like norbornene. Phosphinites are not useful ligands for asymmetric hydrocyanation reactions catalysed by zerovalent palladium complexes. Chelating asymmetric phosphines provide catalysts with better stereoselectivity. It would appear worthwhile to examine the utility of some of the many other chelating asymmetric phosphines available. It must be emphasized that the stereoselectivity claimed for the asymmetric addition of HCN to norbornene catalysed by $Pd(DIOP)_2$ is poorer than originally surmised.

REFERENCES

1. J.A. Osborn, F.J. Jardine, J.F. Young and G. Wilkinson, _J. Chem. Soc._ (A), 1711, (1966).

2. S. Montelatici, A. Van der Ent, J.A. Osborn and G. Wilkinson, _J. Chem. Soc._ (A), 1954, (1968).

3. D. Valentine and J.W. Scott, _Synthesis_, 329, (1978).

4. _U.S. Pat._, 40,08,281, _Chem. Abstr._, 83, 164367, (1975).

5. (a) J.D. Morrison, R.E. Burnett, A.M. Aguiar, C.J. Morrow and C. Phillips, _J. Amer. Chem. Soc._, 93, 1301, (1971).
   (b) T.P. Dang and H.B. Kagan, _J. Chem. Soc. Chem. Commun._, 481, (1971).

6. R.H. Grubbs and R.A. DeVries, _Tet. Lett._, 1879-80, (1977).

7. K. Tani, _Angew. Chem. Int. Ed. Engl._, 24, 217, (1985).

8. R. Noyori, _Tetrahedron_, 40, 1245, (1984).

9. W.R. Jackson and P.S. Elmes, _Aust. J. Chem._, 35, 2041-51, (1982).

10. M. Hodgson and D. Parker, _J. Organometal. Chem._, 325, C27-30, (1987).

11. M. Tanaka and I. Ogata, _J. Chem. Soc. Chem. Commun._, 735, (1975).

12. T. Hayashi, M. Tanaka and I. Ogata, _Tet. Lett._, 295, (1977).

13. W.R. Cullen and Y. Sugi, _Tet. Lett._, 1635, (1978).

14. R. Jackson and D.V. Thompson, _J. Organometal. Chem._, 159, C29, (1978).

15. T.H. Johnson and G. Rangarajan, _J. Org. Chem._, 45, 62, (1980).

16. T.H. Johnson, D.K. Pretzer, S. Thomen, V.J.K. Chaffin and G. Rangarajan, J. Org. Chem., 44, 1878-9, (1979).

17. J. Bourson and L. Oloveros, J. Organometal. Chem., 229, 77-84, (1982).

18. F. Petit, A. Mortreux and M. Petit, Nouv. J. Chim., 7, 593-6, (1983).

19. W.R. Jackson and C.G. Lovel, Aust. J. Chem., 35, 2069-75, (1982).

20. D.H. Valentine, U.S. Pat. 4,115,417, (1978).

21. H. Brunner and J. Doppelberger, Chem. Ber., 111, 673-691, (1978).

22. M. Crutchfield, V. Mark, C. Duncan and J.V. Wazer, Topics in Phosphorus Chemistry, 5, (1967).

23. D.E.C. Corbridge, "Studies in Inorganic Chemistry, 6, Phosphorus", Elsevier, 2nd Ed. (1980).

24. F. Ramirez, O.P. Madan and C.P. Smith, Tetrahedron, 22, 567, (1966).

25. A.H. Cowley, M.J.S. Dewar and W.R. Jackson, J. Amer. Chem. Soc., 92, 5206-13, (1970).

26. J.R. Holden and N.C. Baenziger, Acta Cryst., 9, 194, (1956).

27. J.M. Jenkins and J.G. Verkade, Inorg. Synth., 11, 108, (1968).

28. S.O. Grimm and R.L. Keiter, Inorg. Chim. Acta, 4, 56, (1970).

29. S.O. Grimm, R.L. Keiter and W. McFarlane, Inorg. Chem., 6, 1133, (1967).

30. P.S. Elmes and W.R. Jackson, <u>Ann. N.Y. Acad. Sci.</u>, <u>333</u>, 225, (1980).

31. D.J. Dawson and R.D. Gless, <u>J. Amer. Chem. Soc.</u>, <u>98</u>, 5996, (1976).

32. C.A. Tolman, R.J. McKinney, W.C. Seidel, J.D. Druliner and W.R. Stevens, <u>Adv. Catal.</u>, <u>33</u>, 1, (1985).

33. J.A. Berson and D.A. Ben-Efraim, <u>J. Amer. Chem. Soc.</u>, <u>81</u>, 4083, (1959).

34. D. Parker, <u>J. Chem. Soc. Perkin Trans. II</u>, 83, (1983).

35. W. Brugel, "Handbook of NMR Spectral Parameters", Heyden, London, (1979).

36. G.L. Baker, S.J. Fritschel, J.R. Stille and J.K. Stille, <u>J. Org. Chem.</u>, <u>46</u>, 2954-60, (1981).

37. I. Ojima, T. Kogure and N. Yoda, <u>J. Org. Chem.</u>, <u>45</u>, 4728-39, (1980).

38. <u>Org. Synth.</u>, <u>57</u>, 122, (1977).

39. L.A. Carpino, B.A. Carpino, P.J. Crowley, C.A. Giza and P.H. Terry, <u>Org. Synth. Coll. Vol.</u>, <u>5</u>, 157, (1973).

40. P.L. Flynn, R.E. Zelle and P.A. Grieco, <u>J. Org. Chem.</u>, <u>48</u>, 2424-26, (1983).

41. M. Itoh, D. Hagiwara and T. Kamiya, <u>Bull. Chem. Soc. Jap.</u>, <u>50</u>, 718-721, (1977).

42. A. Carroy, C.R. Langrick, J.M. Lehn, K.E. Matthes and D. Parker, <u>Helv. Chim. Acta</u>, <u>69</u>, 580-6, (1986).

43. W.S. Knowles, M.J. Sabacky and B.D. Vineyard, <u>Adv. Chem. Ser.</u> No. 132, 274, (1974).

44. (a) H.B. Kagan, N. Langlois and T.P. Dang, <u>J. Organomet.</u> <u>Chem.</u>, <u>90</u>, 353-365, (1975).

(b) D. Sinou and H.B. Kagan, <u>J. Organomet. Chem.</u>, <u>114</u>, 325-337, (1976).

45. C.A. Tolman, W.C. Seidel, J.D. Druliner and P.J. Domaille, <u>Organometallics</u>, <u>3</u>, 33-38, (1984).

46. J.M. Brown and R.G. Naik, <u>J. Chem. Soc. Chem. Commun.</u>, 348-50, (1982).

47. J.M. Brown and P.A. Challoner in L.H. Pignolet, "Homogeneous Catalysis with Metal Phosphine Complexes", Plenum, New York, (1983).

48. C. Detellier, G. Gelbard and H.B. Kagan, <u>J. Amer. Chem.</u> <u>Soc.</u>, <u>100</u>, 7556-7561, (1978).

49. W.R. Jackson and C.G. Lovel, <u>Aust. J. Chem.</u>, <u>35</u>, 2053-67, (1982).

50. J.M. Brown, S.J. Cook and S.J. Kimber, <u>J. Organomet. Chem.</u>, <u>269</u>, C58-60, (1984).

51. (a) J. Oku, N. Ito and S. Inoue, <u>Makromol. Chem.</u>, <u>180</u>, 1089-91, (1979).

(b) J. Oku and S. Inoue, <u>J. Chem. Soc. Chem. Commun.</u>, 229, (1981).

(c) W. Bechov and E. Pfeil, <u>J. Amer. Chem. Soc.</u>, <u>88</u>, 4299, (1966).

52. J. Oku, N. Ito and S. Inoue, <u>Makromol. Chem.</u>, <u>183</u>, 579-586, (1982).

CHAPTER 3

STUDIES OF THE MECHANISM OF ASYMMETRIC HYDROCYANATION

3.1. INTRODUCTION

The mechanism of catalytic hydrocyanation by zerovalent metal complexes was not well studied until the early 1980's. Prior to this, mechanistic schemes which appeared were speculative and based on related chemistry, [1,2]. In 1981, Backvall and Andell reported that addition of HCN to 3,3-dimethylbutene catalysed by nickel(0) tetrakis triphenylphosphite was stereospecifically <u>cis</u> [3]. This was also shown to be the case for the reaction catalysed by $Pd(DIOP)_2$ [4]. Tolman at DuPont had studied the chemistry of nickel(0) complexes during the mid 1970's, including the dissociation of NiL_4 complexes, the oxidative addition of HCN to NiL_n, and the reactions of olefins and nitriles with NiL_n complexes. Although these investigations were prompted by their interest in the DuPont adiponitrile process, their first publication suggesting a mechanism for catalytic hydrocyanation of olefins by nickel(0) phosphite complexes appeared in 1984 [5]. Further mechanistic studies have appeared thereafter [6,7] all of which deal with nickel(0) phosphite catalysed hydrocyanation reactions.

A full understanding of the mechanism of a reaction requires a knowledge of the intermediate species involved together with kinetic information relating to the rates of formation and reaction of these species. The number and complexity of reactions in a multi-step catalytic cycle often deters an overall kinetic analysis, the number of variables being too large to distinguish one mechanism from another. The reaction must be analysed in stages, by examining the behaviour

of species at each step in the cycle. Here a difficulty arises
in that species which are observable in the catalytic system may
not necessarily be involved in the kinetically significant
catalytic cycle. For example in the hydrogenation of olefins
catalysed by Wilkinson's catalyst ($RhClL_3$), five rhodium
complexes can be identified or isolated [8], but none of these
complexes is involved in the catalytic cycle, and the
accumulation of any of them actually reduces the overall
reaction rate [9]. Thus the characterisation of complexes in
the catalytic system, while very important, must be combined
with kinetic studies which indicate the importance of the
characterized species.

3.2.   MECHANISTIC STUDIES OF THE Pd(DIOP)$_2$ SYSTEM

One system chosen for study was the Pd(DIOP)$_2$ catalysed
hydrocyanation of olefins. The only previous mechanistic
studies of this system were by Jackson [4] who showed that the
addition of HCN was stereospecifically cis. Chaloner [10] had
independently demonstrated that the correct formula for the
complex was tetrahedral Pd(DIOP)$_2$, not "Pd DIOP" as Jackson had
originally suggested [11]. Chaloner also described the changes
in the ^{31}P spectrum of the complex (in toluene) with
temperature, on cooling, an A_2B_2 spectrum was obtained which
collapsed to a singlet as the temperature was raised. This was
ascribed to exchange between different conformations of the
seven-membered chelate rings. Finally, Chaloner monitored the
reaction of the complex with several electron-poor alkenes to
give DIOP palladium alkene complexes.

3.2.1. Generation of Pd(DIOP)$_2$

The complex Pd(DIOP)$_2$, for the initial N.M.R. studies was generated in situ from Pd dba$_2$ or Pd$_2$dba$_3$.C$_6$H$_6$ and DIOP. Toluene and benzene were used as solvents: where low temperature studies were required toluene was used. The solutions of the complex were typically 0.01 to 0.02 molar. This compared with a 3.6 x 10^{-3} M concentration of the complex and a 0.02 M concentration of free DIOP in an actual hydrocyanation reaction. In order to confirm that the complex formed was the same as the preformed Pd(DIOP)$_2$ studied by Chaloner, and to show that the presence of the displaced dba ligands did not interfere with the system, the temperature dependence of the ^{31}P N.M.R. spectrum was studied. Similar changes in the ^{31}P spectrum to those reported by Chaloner were observed. A comparison of the data is given in Table 1.

The equations used for determining the rate constant for exchange k, were as follows, [12,13]:

(i) <u>slow and intermediate exchange</u>

$$k = \pi[(\omega_{\frac{1}{2}})_e - (\omega_{\frac{1}{2}})_0]$$

$$\text{and} \quad k = \frac{\pi}{\sqrt{2}} (\Delta\nu_0{}^2 - \Delta\nu_e{}^2)^{\frac{1}{2}}$$

(ii) <u>fast exchange</u>

$$k = \frac{\pi\Delta\nu_0{}^2}{2}[(\omega_{\frac{1}{2}})_e - (\omega_{\frac{1}{2}})_0]^{-1}$$

where k = rate of exchange.

$(\omega_{\frac{1}{2}})_0$ = linewidth at half height in the absence of exchange

$(\omega_{\frac{1}{2}})_e$ = linewidth at half height of broadened peak

$\Delta\nu_0$ = Peak separation in the absence of exchange

$\Delta\nu_e$ = Peak separation in the exchange broadened spectrum.

TABLE 1. Temperature dependence of ^{31}P N.M.R. spectrum of
Pd(DIOP)$_2$ generated in situ from Pd dba$_2$:
A comparison with literature[10] values

Experimental			Literature	
T(K)	$\omega_{\frac{1}{2}}$(Hz)	k(s^{-1})	T(K)	k(s^{-1})
293	16	240,000		
273	43	70,000	277	60,000
263	112	24,500		
252	157	17,500	252	18,000
232	376	1,182	228	1,750
215	77	226	215	290
			203	65
			190	35

The agreement between the observed and published values of
the rate constant is close, considering that a computer program
[14] was used to fit the literature values.

In some later experiments, Pd(DIOP)$_2$ was generated using
DIOP to displace ethene from the novel complex DIOP palladium
ethene, the preparation of which is described later (section
3.5). The temperature dependence of the ^{31}P N.M.R. spectrum of
the complex formed thereby was identical to that of samples of
Pd(DIOP)$_2$ prepared by adding DIOP to Pd$_2$(dba)$_3$.C$_6$H$_6$ or Pd dba$_2$.

3.2.2. Reactions of Pd(DIOP)$_2$

(i) With alkenes. As outlined in the introduction, (section
1.4.2.), the formation of many nickel/phosphorus ligand/alkene

complexes has been observed from reaction of olefins with NiL_3 or NiL_4 [15,16], or by substitution of ethene in $C_2H_4NiL_2$ complexes [17]. Not all of these complexes were isolated, and many were characterised and studied by their ^{1}H and [31]P N.M.R. spectra, or by their electronic spectra.

Chaloner and Brown formed DIOP palladium alkene complexes which were not isolated but identified in solution by [31]P N.M.R. These complexes were formed by addition of alkenes to solutions of $Pd(DIOP)_2$ in toluene. The percentage of palladium converted to alkene complex by addition of varying amounts of excess alkene depended on the electronic and steric properties of the alkene. Thus (E)-(CN)HC=CH(CN) gave 100% conversion of $Pd(DIOP)_2$ to DIOP Pd(Alkene) upon addition of one equivalent of alkene, whereas di-t-butylfumarate gave only a 10% conversion when present in five-fold excess. Other alkenes used were $CF_3FC=CFCF_3$, dimethylmaleate, maleic anhydride, dimethyl and diethyl fumarate [10]. Tolman has suggested that electronic rather than steric effects governed the stability of olefin $Ni[P(o-o-tolyl)]_2$ complexes [15].

Solutions of $Pd(DIOP)_2$ in toluene were exposed to various alkenes in the hope of forming (DIOP)Pd(Alkene) complexes, suitable for studying the effects of HCN on these species.

The investigations involved addition of at first one equivalent of alkene to a cooled solution of $Pd(DIOP)_2$. The [31]P N.M.R. of the solution was observed in the range 215 to 312 K. The experiments were repeated with five or ten equivalents of alkene added, and finally with a large excess of added alkene. Of the alkenes used, vinyl acetate, norbornene, (E) and (Z)

2-butenenitrile and 1-tetradecene all failed to change the ^{31}P spectrum at any temperature or concentration indicating that no displacement of DIOP from Pd(DIOP)$_2$ had occurred. The highly electron-poor alkene TCNE quantitatively displaced DIOP from Pd(DIOP)$_2$. This was indicated by loss of the Pd(DIOP)$_2$ resonances from the ^{31}P N.M.R. spectrum, and the appearance of two new resonances, one at the position of free DIOP, the other at δ^{31}P +8.8 due to a (DIOP)Pd TCNE complex. Thus in solutions containing Pd(DIOP)$_2$ and alkene the formation of a DIOP palladium alkene complex is only observed with electron poor alkenes. As already noted, (section 1.2.4,c) many electron-poor alkenes are not hydrocyanated by nickel phosphite complex based catalyst systems, possibly due to the stability of the intermediate alkene complexes inhibiting oxidative addition, and any further reaction.

(ii) <u>With HCN</u>. Tolman and co-workers have shown that HCN oxidatively adds to NiL$_3$ (L = P(o-o-tolyl)$_3$) to give HNiL$_3$CN and that this hydride complex reacts with ethene to give alkylnickel cyanide species [5].

HCN was added (3 to 200 equivalents) to solutions of Pd(DIOP)$_2$ both in the presence and absence of alkenes and in the temperature range 215 to 285 K. No hydride signals were observed in the ^{1}H spectrum, and no change in the ^{31}P spectrum was observed, apart from the gradual appearance of sharp signals at δ^{31}P 16.7 and 30.0 at higher temperatures. After several weeks, Pd(DIOP)$_2$ resonances were no longer seen in the ^{31}P N.M.R. spectrum, and material had precipitated from solution. The spectrum showed only the δ16.7 and 30.0 resonances which

were tentatively assigned to DIOP Pd(CN)$_2$ and DIOP oxide respectively. The assignment of the $\delta 30.0$ signal to DIOP oxide was confirmed by treating some DIOP with hydrogen peroxide and adding the colourless solid formed to the reaction solution, which greatly increased the intensity of this resonance. The precipitate is likely to be Pd(CN)$_2$, formed in an analogous manner to Ni(CN)$_2$ obtained from solutions of nickel phosphorus complexes exposed to HCN [5], Scheme 1.

$$Pd(DIOP)_2 + 2HCN \longrightarrow (DIOP)Pd(CN)_2 + H_2 + DIOP$$

$$(DIOP)Pd(CN)_2 \longrightarrow Pd(CN)_2 + DIOP$$
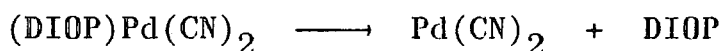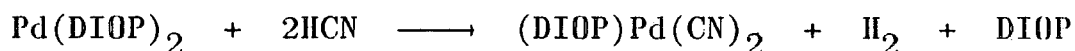
Scheme 1

(iii) With nitriles. Tolman has described the formation of nitrile complexes of nickel from various phosphorus ligands and nitriles. He determined the stoichiometry of the reaction (Scheme 2) by ^{31}P N.M.R. spectroscopy. Gradual addition of n-C$_4$H$_9$CN to a solution of Ni[P(o-o-tolyl)$_3$]$_3$ moved the ^{31}P N.M.R. resonance from 128.5 ppm of NiL$_3$. Addition of one equivalent of n-C$_4$H$_9$CN moved the resonance to 130.7 ppm. Further additions of n-C$_4$H$_9$CN did not alter the ^{31}P N.M.R. spectrum. Addition of P(o-o-tolyl)$_3$ to the system gave a resonance at 130 ppm, due to free phosphite. Thus the exchange of nitrile in Scheme 2 is fast, but exchange of phosphite with the nitrile complex is very slow [18].

$$RCN \; + \; NiL_3 \; \rightleftharpoons \; (RCN)NiL_3 \qquad fast$$
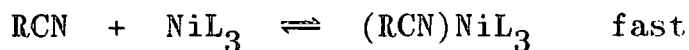
Scheme 2

Values for the equilibrium constants for nitrile complex formation were determined spectrophotometrically. The formation of nitrile complex was high for ligands which tend to dissociate from NiL_4 complexes e.g. PPh_3, $P(o\text{-}o\text{-}tolyl)_3$, but was low for ligands which form stable NiL_4 complexes in solution e.g. $P(OEt)_3$.

Pd(DIOP)$_2$ was exposed to various concentrations of acetonitrile, butenenitrile, norbornane carbonitrile and acetone cyanohydrin. The ^{31}P N.M.R. spectrum was unchanged in all experiments. Pd(DIOP)$_2$ is a solution stable species therefore the lack of any detectable nitrile complexes is expected from Tolman's studies.

3.3. THE USE OF DIOP PLATINUM ETHENE AS A MODEL IN MECHANISTIC STUDIES

The low reactivity of Pd(DIOP)$_2$ necessitated a search for a relevant, more reactive system to study. The complexes of third row elements tend to be kinetically more inert than analogous complexes of the second row elements. A consequence of this is that third row complexes often react too slowly to be useful as

homogeneous catalysts, although the slower reactions facilitate
mechanistic studies by allowing the observation of intermediates
which may be too unstable to observe in second row systems. The
possibility of following the course of a reaction is also
increased, as opposed to simply observing the products.

The preparation of the platinum complex DIOP platinum
ethene 1 has been described by Brown and co-workers [19]. The
complex is prepared by borohydride reduction of DIOP $PtCl_2$ in
ethanol/CH_2Cl_2 under an ethene atmosphere. The complex is a

1
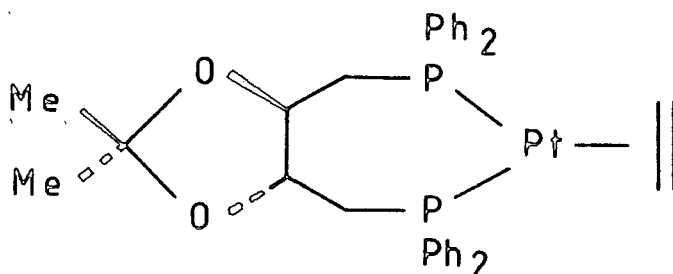
stable white solid, which is soluble in various organic solvents
including CH_2Cl_2, benzene and toluene. Brown also noted the
facile displacement of ethene from the complex by, for example,
CO or allene.

Thus, despite the fact that $Pt(DIOP)_2$ does not catalyse the
addition of HCN to norbornene to any appreciable extent [4], (it
was subsequently found that DIOP Pt ethene is also unable to
catalyse the reaction) (section 2.6.6,iv). DIOP Pt ethene was a
useful starting material to generate and study possible

intermediates; species analogous to those which may be involved
in the mechanism of the $Pd(DIOP)_2$ catalysed hydrocyanation of
alkenes. The study of the more kinetically inert platinum
analogues of palladium complexes has often been advocated
[20,21].

Platinum complexes have an added advantage over palladium
complexes in that information from [195]Pt-^{31}P and [195]Pt-[1]H
coupling may be deduced directly from [31]P N.M.R. spectra, giving
extra structural information. This extra splitting can
sometimes be undesirable for certain resonances which are less
readily observed, e.g. metal hydride resonances in [1]H N.M.R.
spectra.

3.3.1. Reactions of DIOP Platinum Ethene

(i) With alkenes. Addition of ethene to solutions of DIOP
platinum ethene in d^6 benzene gave a sharp new resonance in the
[1]H spectrum, at the position of free ethene. The resonances due
to bound ethene remained unaltered. Further additions of ethene
simply increased the intensity of the free ethene signal.
However, addition of norbornene or norbornadiene to solutions of
DIOP platinum ethene in CH_2Cl_2, benzene or toluene caused a
change in the [31]P N.M.R. spectrum. Signals due to DIOP platinum
ethene (δ_P +13.7 [1]J_{P-Pt} 3585 Hz) disappeared, and were replaced
by new resonances with δ_P +15.8, [1]J_{P-Pt} 3414 Hz for norbornene
and δ_P +14.6, [1]J_{P-Pt} 3251 Hz for norbornadiene. These
resonances were assigned to the DIOP platinum alkene complexes 2
and 3 respectively.

$\underline{2}$ $\underline{3}$
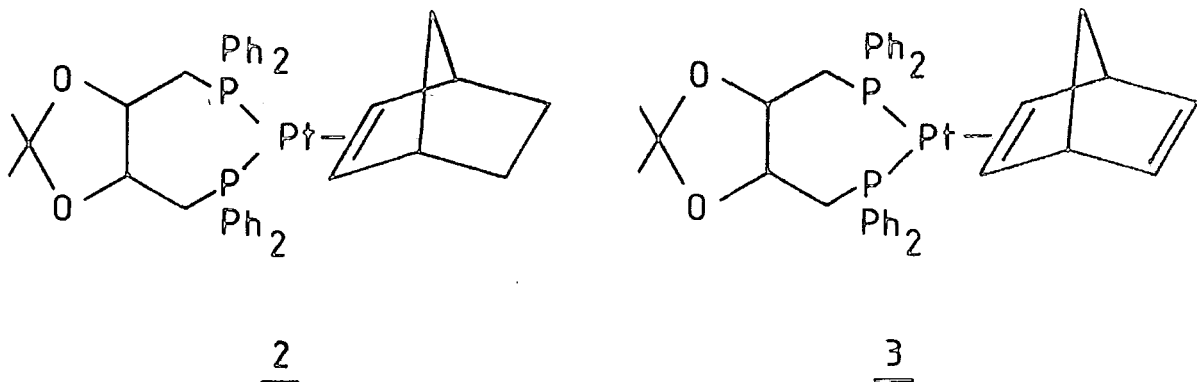
Thus exchange of alkene in $\underline{1}$ is slow on the N.M.R. timescale. Previous work by Tolman [16] with monophosphine complexes indicated that the exchange may occur via an associative mechanism.

The complexes $\underline{2}$ and $\underline{3}$ were isolated by treating $\underline{1}$ with excess alkene in THF, followed by removal of the ethene. solvent and unreacted excess alkene in vacuo. The ^{1}H N.M.R. spectra of $\underline{2}$ in toluene is shown in **Figure 1**. The coordinated alkene protons resonate at δ^1H 2.9 ppm and 2.75 ppm compared to δ6.0 ppm for the free alkene. **Figure 2** shows the ^{1}H N.M.R. spectrum of $\underline{3}$ in toluene. The bound olefin protons of norbornadiene resonate at δ3.29 and δ3.25. Norbornadiene is coordinated to platinum by only one olefinic bond. The non-coordinated olefinic protons of bound norbornadiene resonate at δ6.74 and δ6.86, compared to δ6.86 ppm for free norbornadiene olefinic protons. Both norbornene and norbornadiene are bound diastereoisomerically by the exo face.

(ii) **With HCN**. Addition of a ten-fold excess of HCN to a 40 mM solution of $\underline{1}$ in d_8 toluene at room temperature gave a colourless solution, the ^{31}P N.M.R. spectrum of which consisted

Figure 1: [1]H N.M.R. SPECTRUM OF

DIOPPLATINUM NORBORNENE
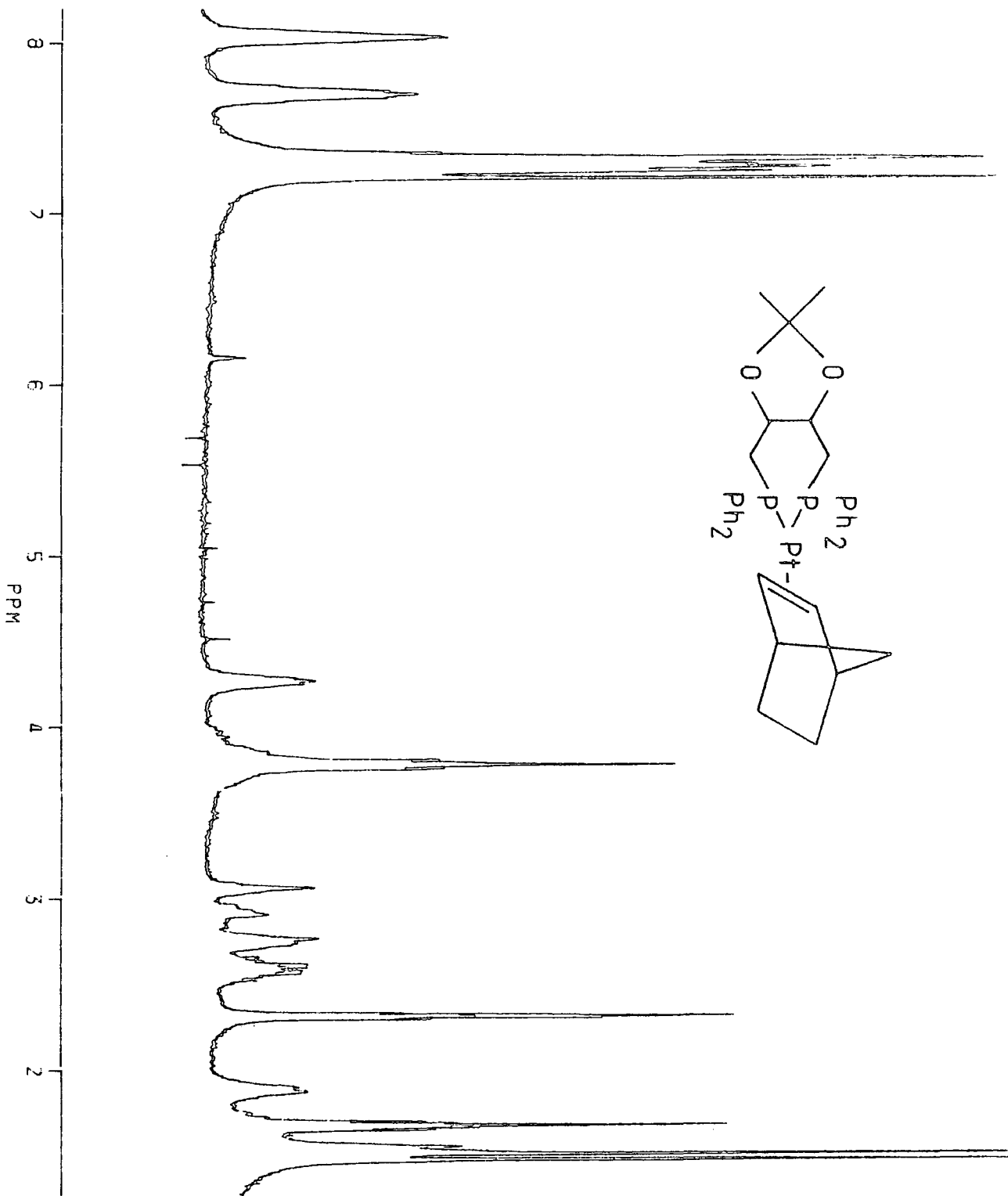
Figure 2. PROTON N.M.R. SPECTRUM OF
DIOP PLATINUM NORBORNADIENE,
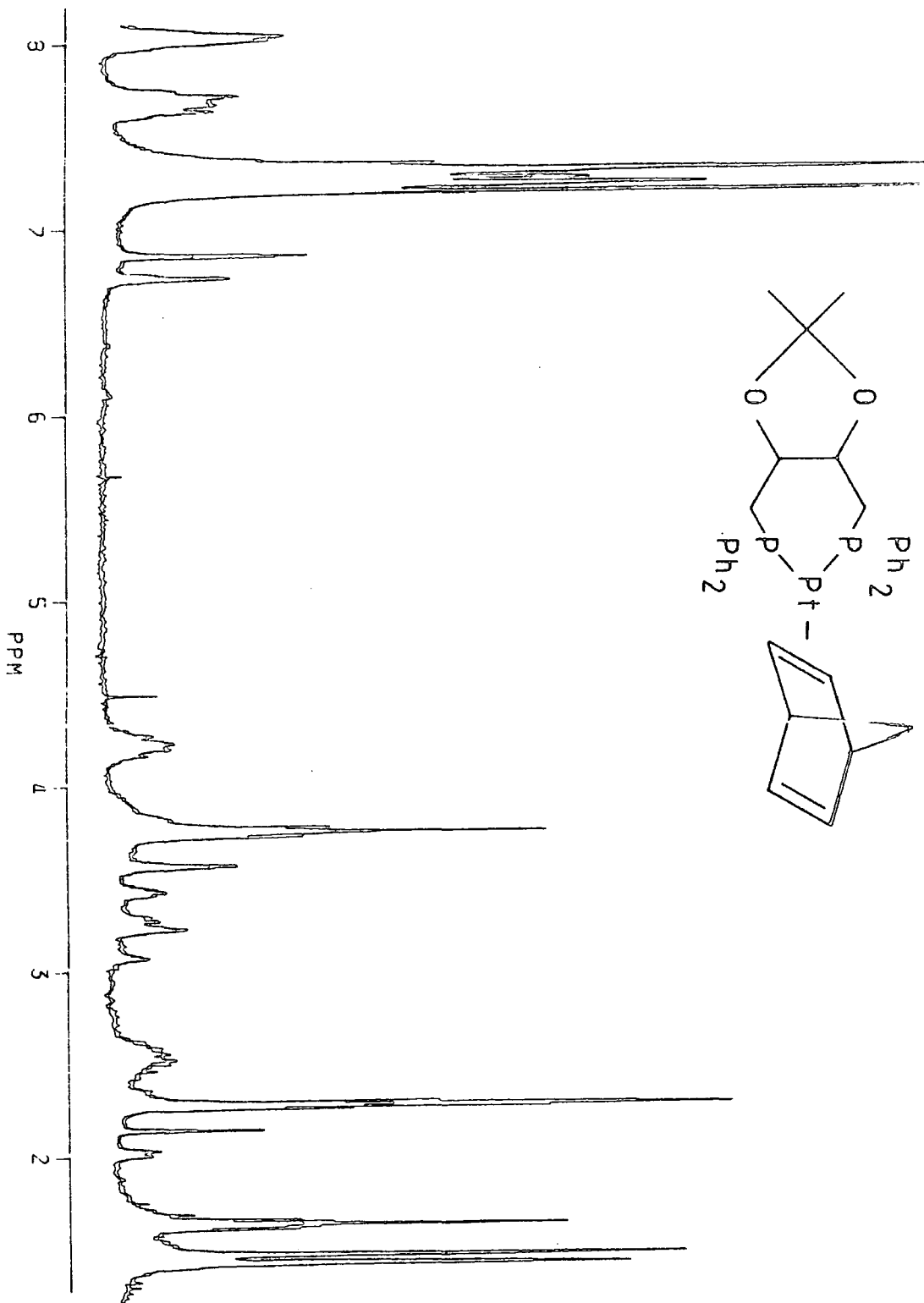
of two platinum coupled doublets δ_{Pa} 5.4 $^1J_{PtPa}$ 2840 Hz, δ_{Pb} 4.1 ppm $^1J_{PtPb}$ 1725 Hz, $^2J_{PaPb}$ 17 Hz. The ^1H spectrum of the same solution clearly showed a hydride resonance, with an integrated intensity of one proton. If care was taken to exclude air during manipulations, the resonances were unchanged for a week at 5^{0}C. Further HCN additions simply increased the intensity of the resonance due to HCN in the ^1H spectrum. The ^{31}P N.M.R. spectrum was unaltered. The N.M.R. spectral data is consistent with the formation of a hydridocyanide complex, 4, as shown in Scheme 3.
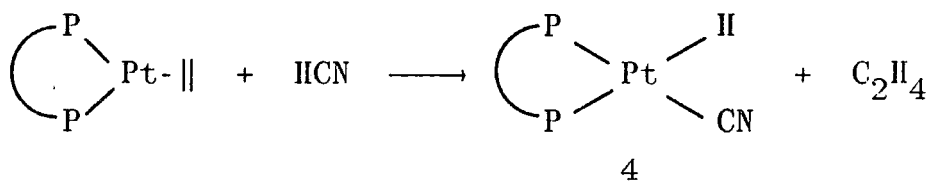
Scheme 3

The ^1H data compared well with the ^1H data for the isoelectronic DIOP Pt hydride 5 described by Brown [19].

The values of $^1J_{P,Pt}$ obtained from the ^{31}P spectra are particularly useful for structural information. Whereas the theories of interpretation of chemical shifts and indirect couplings are complicated by uncertainties, and in the case of ^2J, by several terms of different sign [22], the theory of coupling between directly bonded atoms is well established. The expression for $^1J(PtP)$ is given by

$$^1J_{P,Pt} \; \alpha \; \gamma_{Pt}\gamma_{P}(\Delta E)^{-1}\alpha_{Pt}{}^2\alpha_{P}{}^2|\psi_{Pt(6S)}(0)|^2|\psi_{P(3S)}(0)|^2$$

[1]H N.M.R. CD_2Cl_2 [19] -58^oC

δ-3.3 ppm

[2]J(HP) = 18 (cis)

160 (trans)

[1]J(HPt) 844 Hz

5

[1]H N.M.R. C_7D_8 15^oC

δ-4.02 ppm

[2]J(HP) = 16 (cis)

187 (trans)

[1]J(HPt) = 967 Hz

4

where γ_{Pt} and γ_P are magnetogyric ratios

ΔE is the average excitation energy

α_x^2 is the s character of the orbital used by x in the Pt-P bond and

$|\psi(0)|^2$ terms are the electron densities at the parent nuclei, [23].

Pidcock and co-workers have examined a series of platinum phosphine complexes and have shown that ΔE^{-1} is not an important term, and also that α_P^2 and $|\psi_{P(3S)}(0)|^2$ are constant for a given phosphine. Thus differences between $^1J_{PPt}$ coupling constants for Pt(II) complexes are due to differences in the S character of the Pt-P bond, which is mainly determined by the nature of the ligand _trans_ to phosphorus [24]. $^1J_{PPt}$ gives a measure of the trans influence of a ligand. The trans influence is a weakening of the bond between platinum and the trans ligand, transmitted through the σ framework of the complex. The effect is thought to arise by rehybridisation of the platinum σ bonding orbitals depending on the ligand. Calculations support

this explanation [25]. Phosphines and hydride are strongly bonding ligands, having a high overlap with the platinum σ orbitals, thus reducing the availability of those bonding orbitals to the trans ligand, thereby weakening the trans bond. The coupling constant decreases with decreasing covalency or s-character in the Pt-P bond. $^1J_{PPt}$ is therefore smaller for ligands with a high trans influence e.g. hydride or alkyl ligands.

In cis-PtMeCl(Et$_3$P)$_2$, $^1J_{PPt}$ for phosphorus trans to chloride is 4180 Hz, and for the phosphorus trans to Me $^1J_{PPt}$ is 1720 Hz [24]. Similar values are observed in the series of complexes Pt(Cl)(CH$_3$)Ph$_2$P(CH$_2$)$_n$PPh$_2$ which have been examined for chelating phosphines with n = 1 to 3. $^1J_{PPt}$ for P trans to chloride is around 3400 Hz and P trans to Me gives $^1J_{PPt}$ of around 1790 Hz, [26]. The ^{31}P N.M.R. data for the complex formed on addition of HCN to DIOP platinum ethene is consistent with the suggested structure 4. The complex contains two non-equivalent phosphorus atoms, one of which is trans to hydrogen (a ligand with a high trans influence) J = 1725 Hz. The other phosphorus atom is trans to cyanide (a ligand with a lower trans influence) J = 2840 Hz. For comparison $^1J_{PPt}$ = 2530 Hz in [PtCN(PEt$_3$)$_3$]$^+$ClO$_4^-$ [27].

3.3.2. Reactions of DIOP Platinum Norbornene

(i) With excess alkene. Preformed DIOP platinum norbornene was stable in toluene at ambient temperatures for several hours. Addition of excess alkene at a wide range of concentrations had

no effect on the ^{31}P spectrum while the ^{1}H spectrum showed sharp resonances due to free and bound alkene. Temperature variation over the range 273 to 305 K did not substantially alter the linewidths either with or without added alkene. The results are an extension of the information obtained from the experiments with DIOP platinum ethene. They indicate that the complex does not dissociate detectably (Scheme 4: K$_2$). Tolman observed the formation of bis olefin complexes at high olefin concentrations, in nickel(0) and platinum(0) systems [15] (olefin > 1 M). No evidence for the formation of such complexes was found in the case of DIOP platinum norbornene [Scheme 4: K$_3$]. However, it does seem likely that exchange may occur slowly in these systems, via an associative mechanism, as observed for other platinum alkene complexes [16].
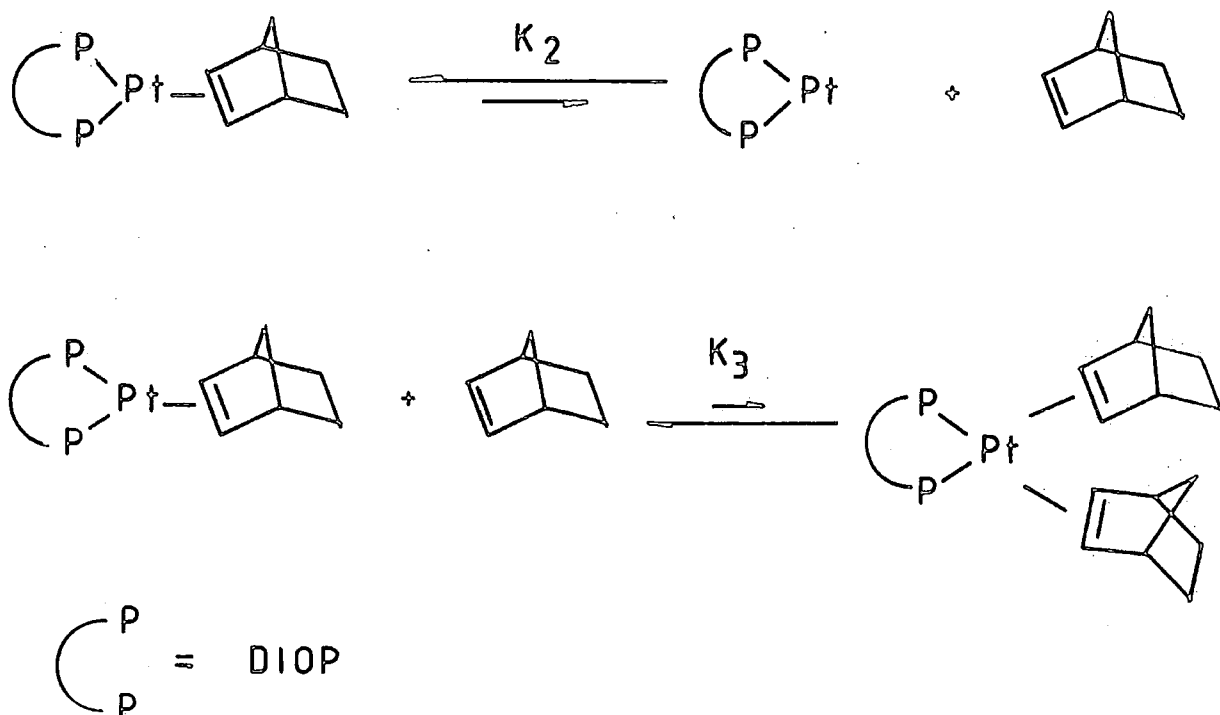
Scheme 4

(ii) <u>With HCN</u>. A fourteen-fold excess of HCN was added to a 35 mM solution of preformed DIOP Pt norbornene in d^8 toluene at 233 K. The spectrum was monitored after 15 minutes, weak signals appeared at $\delta^{31}P$ 5.35 and δ 4.1 ppm alongside the resonance due to DIOP Pt norbornene. As the solution was warmed to 273 K, the signals due to DIOP Pt norbornene vanished and were replaced by two platinum coupled doublets (<u>Figure 3</u>).

$$\delta_{Pa} \text{ 5.35 ppm} \qquad ^1J_{PtPa} \text{ 2840 Hz}$$
$$\delta_{Pb} \text{ 4.1 ppm} \qquad ^1J_{PtPb} \text{ 1725 Hz}$$

After half an hour at 273 K a broad platinum coupled signal began to appear at $\delta 9.0$, J_{PPt} 2320 Hz. On warming to room temperature, the resonance at δ 9.0 began to grow ($t_{\frac{1}{2}} \sim 25$ mins.) at the expense of the other resonances. After 2 days at 278K, the ^{31}P spectrum consisted of the $\delta 9.0$ $^1J_{PPt}$ 2320 Hz signal only. When HCN was added to DIOP platinum norbornene at ambient temperature, the ^{31}P N.M.R. spectrum obtained immediately consisted of only the platinum coupled doublets described above. ^1H N.M.R. spectra of such solutions (<u>Figure 4</u>) contained hydride resonances with the same $^{195}Pt-^1H$ and $^{31}P-^1H$ coupling as observed in the spectra obtained by addition of HCN to DIOP platinum ethene (<u>Figure 5</u>). The ^1H N.M.R. spectrum also showed the appearance of resonances due to free norbornene. Thus the product in both cases is DIOP platinum hydridocyanide <u>4</u>. Free ethene was not observed in the ^1H spectrum on addition of HCN to DIOP platinum ethene; this is probably because of the volatility of the liberated gas. The identity of the species at $\delta 9.0$ is discussed below in section (iii).

(iii) <u>With excess reagents</u>. Tolman [5] and McKinney [7]

Figure 3. PHOSPHORUS N.M.R. SPECTRUM OF DIOP Pt NORBORNENE + HCN
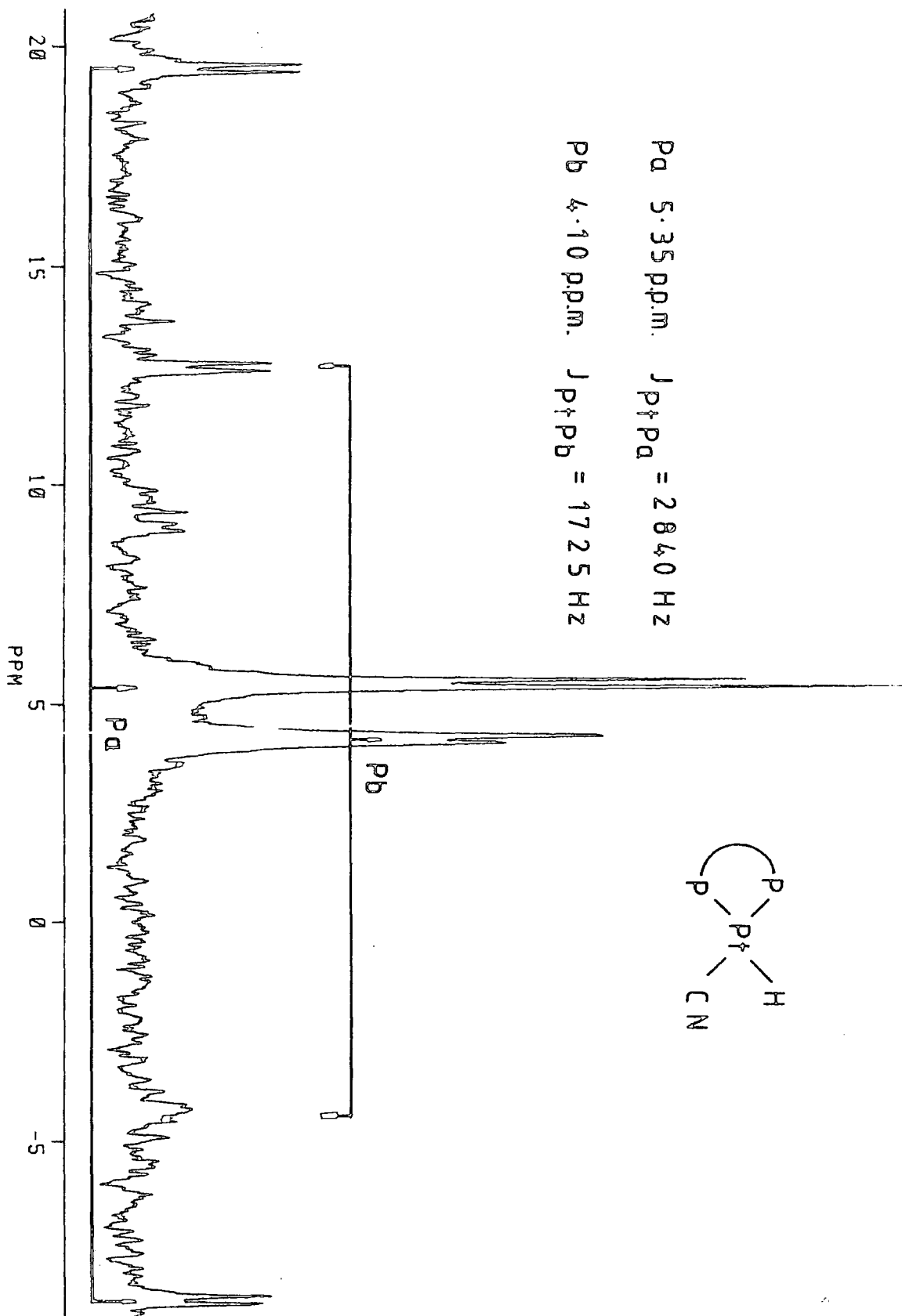
Figure 4. PROTON N.M.R SPECTRUM OF
DIOP Pt NORBORNENE + HCN
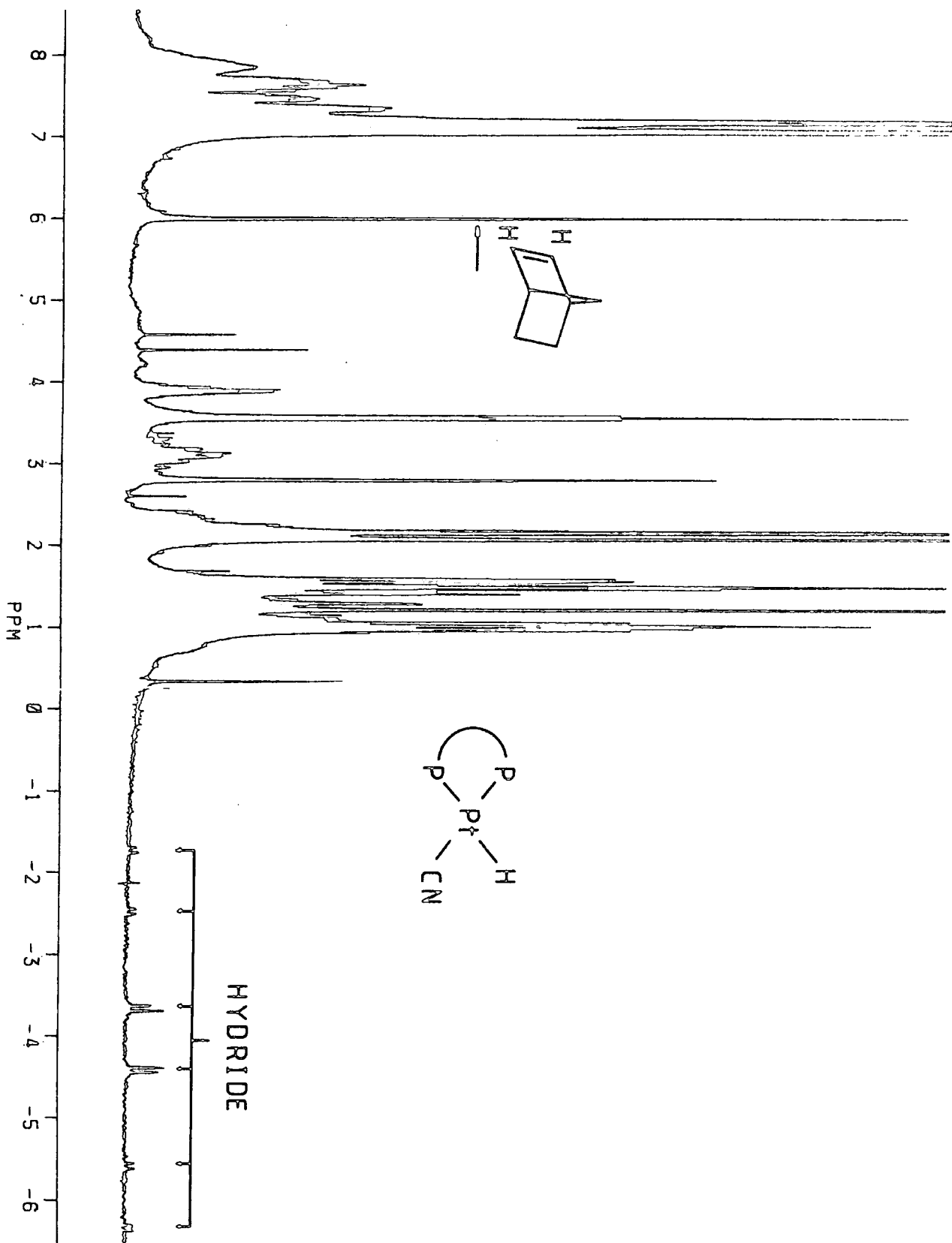
Figure 5. HYDRIDE REGION OF Figure 4.

J_{HPt} = 967 Hz

$J_{HPtrans}$ = 187 Hz

J_{HPcis} = 16 Hz
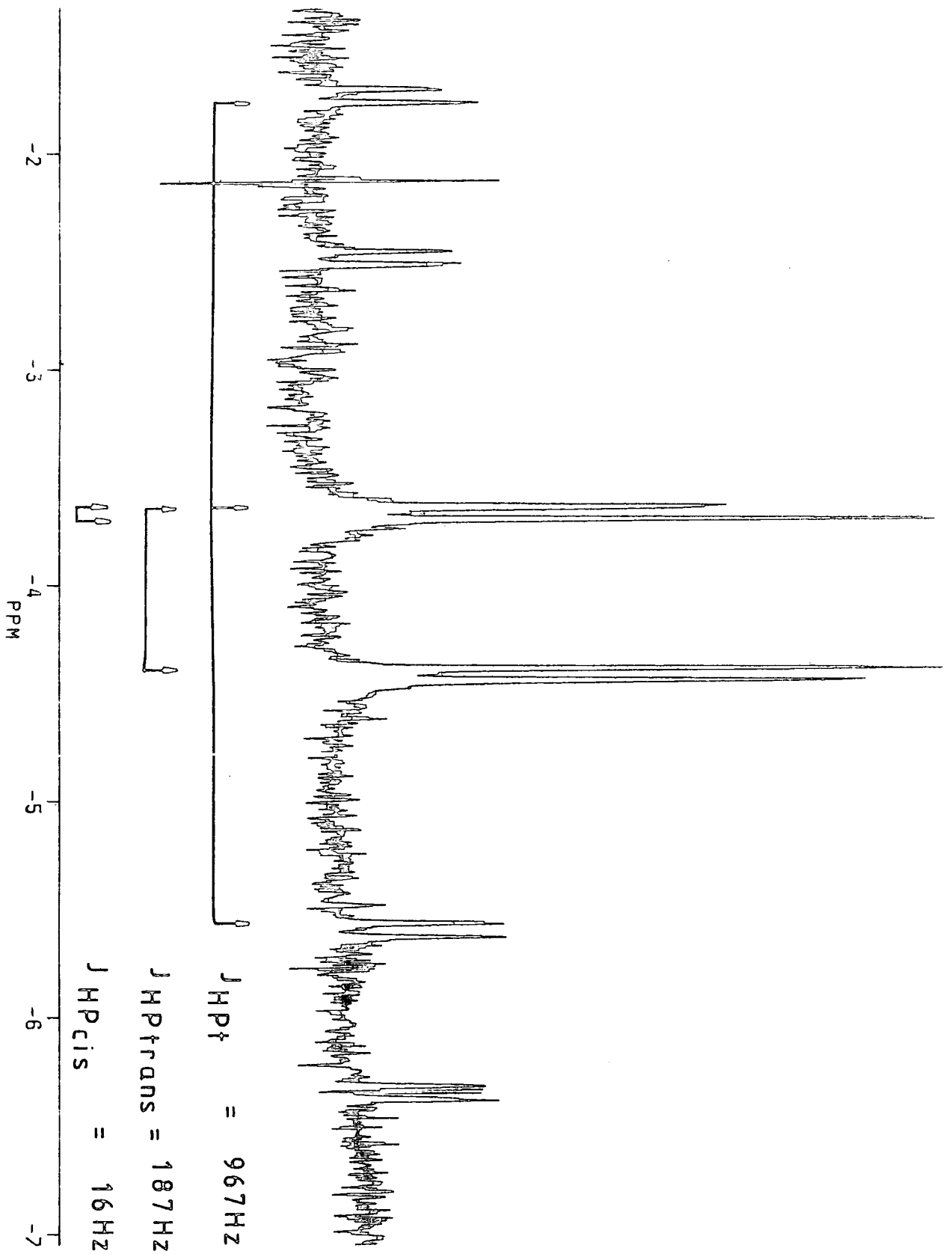
describe the reaction of a nickel hydrido cyanide
HNiCN[P(o-o-tolyl)$_3$]$_3$ with excess alkene (ethene) at -50^{0}C to
give nickel alkyl cyanide complexes. The behaviour of DIOP
platinum hydridocyanide in the presence of excess norbornene
(norbornadiene 3.3.3.iii.) and HCN was accordingly investigated.
The system is more difficult to understand when excess alkene
and/or HCN are present. This is the case under hydrocyanation
reaction conditions. An experiment in which a large excess of
HCN was added to a solution containing DIOP platinum norbornene
gave a complex ^{31}P spectrum containing, in addition to
resonances ascribed to 4:

(a)   sharp platinum coupled singlet δ -5.3 ^{1}J$_{PPt}$ 2400 Hz:

(b)   a sharp platinum coupled triplet δ 8.9 ^{1}J$_{PPt}$ 3100 Hz:

(c)   two sharp doublets δ_{Pa} -0.1 δ_{Pb} -0.9 J$_{P,P}$ 19 Hz for which
      no obvious platinum satellites could be found;

(d)   several other broad resonances.

Figure 6 shows a typical ^{31}P N.M.R. spectrum from the system.

It is interesting to note that in this and subsequent
experiments in which a large excess of alkene was initially
present, formation of the species at δ9.0 with ^{1}J$_{P,Pt}$ 2320 Hz.
was greatly suppressed, not appearing until the system had been
at room temperature for many hours. This fact, and the
magnitude of ^{1}J$_{PPt}$, suggest that the species being formed is
DIOP Pt(CN)$_2$.

Complex mixtures of products were also obtained when
norbornene was added to solutions of 4 generated by addition of
HCN to DIOP Pt ethene. Cooling the reaction mixtures was of
little help. Varying concentrations of HCN and norbornene did

Figure 6. PHOSPHORUS NMR SPECTRUM OF DIOP Pt NORBORNENE + EXCESS HCN & NORBORNENE.
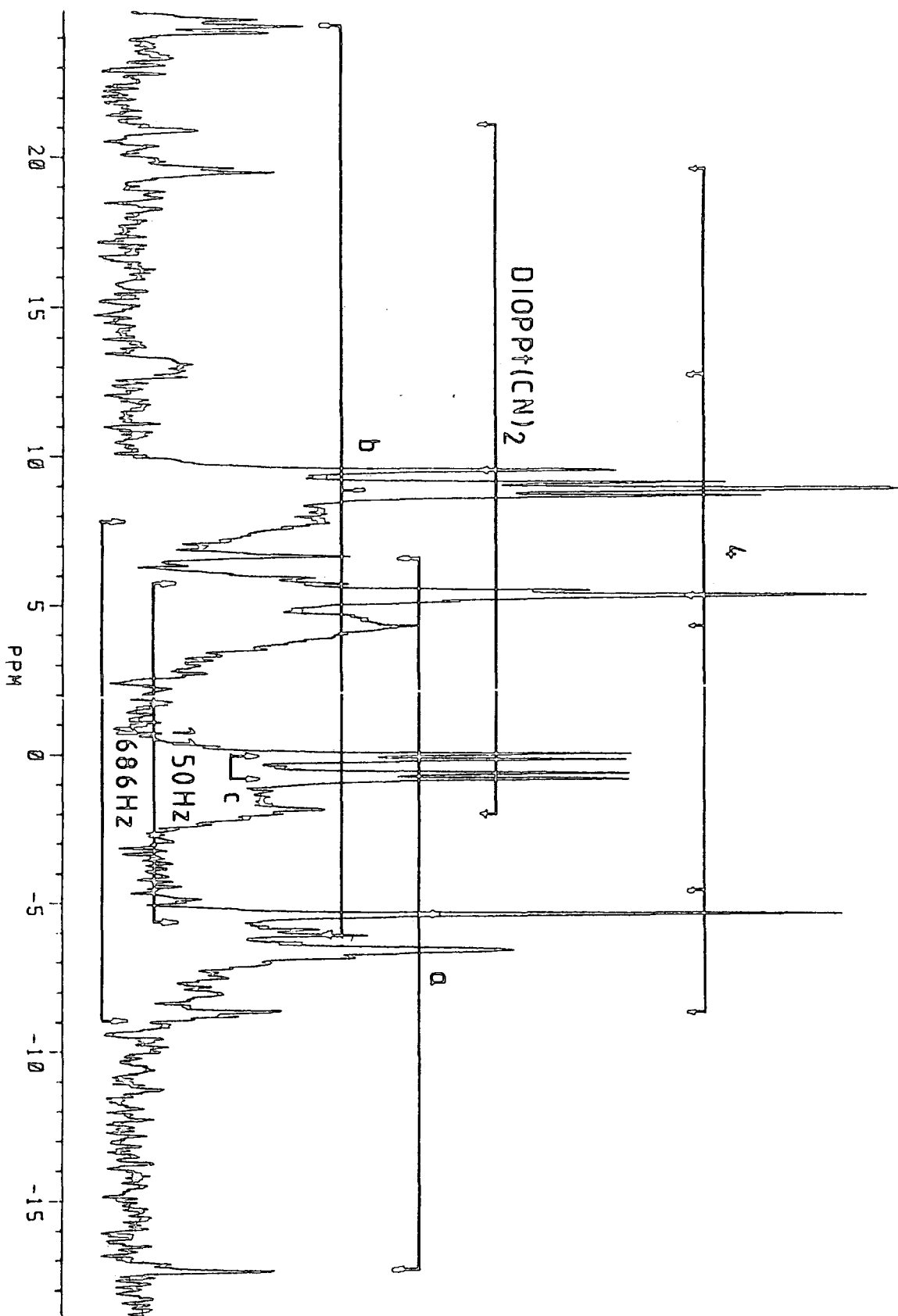
not sharpen lines in the spectra, eliminate or enhance any of the resonances.

The fact that additional species occur only in the presence of excess reagents suggests that they involve reaction of $\underline{4}$ with alkene or HCN. Excess HCN may possibly add to $\underline{4}$ to give an unstable Pt(IV) species $\underline{7}$ (Scheme 5).
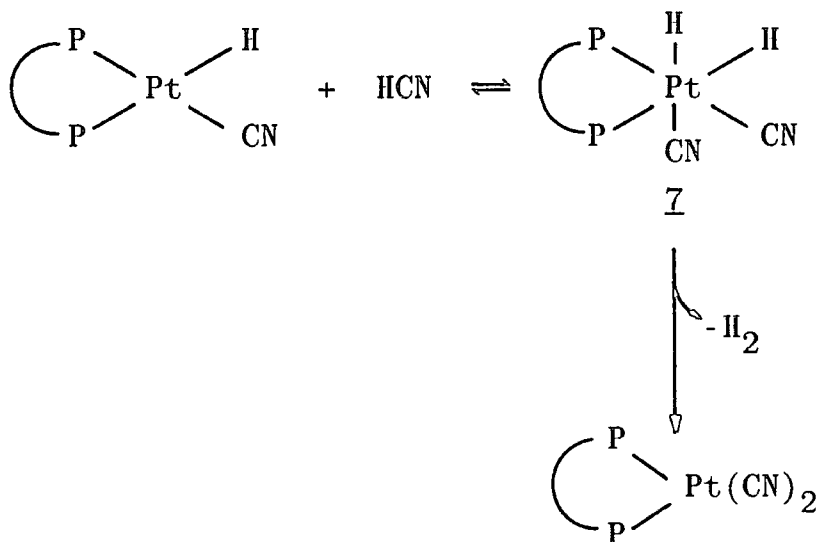
Scheme 5

A related unstable dihydride is formed by the action of dry hydrogen chloride on trans-$[(PEt_3)_2PtHCl]$ in ether [28], Scheme 6.

The value of $^1J_{PPt}$ for platinum(IV) compounds is predicted to be $^2/3$ of the value in a Pt(II) compound due to the sharing of the Pt s orbital by six rather than four ligands. This relationship has been found experimentally [23]. If this also held for (DIOP)PtHCN and "(DIOP)PtH$_2$CN$_2$", the values for $^1J_{PPt}$ could be 2840 x $^2/3$ = 1686 Hz and 1725 x $^2/3$ = 1150 Hz.

$$\text{Et}_3\text{P}\diagdown\underset{\text{H}\diagup\text{Pt}\diagdown}{}\diagup\text{Cl} + \text{HCl} \xrightarrow{\text{ether}} \text{Et}_3\text{P}\diagdown\overset{\text{H}}{\underset{\text{Cl}}{|}}\diagup\text{Cl}$$
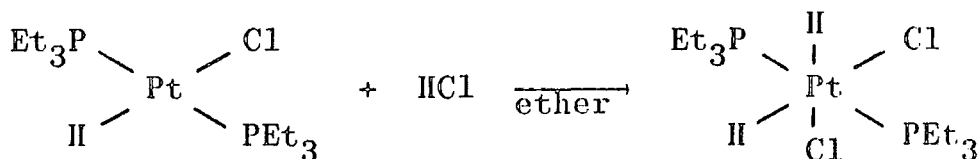
Scheme 6

Platinum satellites drawn onto the system of peaks (c) δ_{P_a} -0.1 ppm δ_{P_b} -0.9 ppm $J_{P,P}$ 19 Hz of $^1J_{PPt}$ 1686 and 1150 Hz are all obscured by other peaks in the actual ^{31}P N.M.R. spectra obtained. Pt satellites for the four sharp signals of (c) would be easily observable in any other part of the spectrum. It is therefore possible that the group of resonances (c) are due to the dihydride 7 with platinum couplings of around 1686 and 1150 Hz obscured by other peaks.

3.3.3. Reactions of (DIOP) Platinum Norbornadiene

(i) **With excess alkene.** As with (DIOP) platinum norbornene no change in the ^{31}P N.M.R. spectrum was observed on altering either the temperature, or the amount of excess alkene added to a solution of the complex.

(ii) **With HCN.** Addition of a ten-fold excess of HCN to (DIOP) platinum norbornadiene (0.035 mM in toluene) at 263 K caused no change in the ^{31}P N.M.R. spectrum. As the sample was warmed to 288 K, resonances of the hydridocyanide complex 4 began to

appear. Unlike (DIOP)Pt ethene and (DIOP)Pt norbornene, in this case, other resonances were present, as two new species appeared at approximately equal rates. These were,

(a) δ_{Pa} 0.25 ppm $^1J_{Pa,Pt}$ 1240 Hz $^2J_{PaPb}$ 5 Hz

δ_{Pb} 0.05 ppm $^1J_{Pb,Pt}$ 1238 Hz

(b) δ_{Pa} 9.9 ppm $^1J_{Pa,Pt}$ 3087 Hz $^2J_{PaPb}$ 19 Hz

δ_{Pb} 7.7 ppm $^1J_{Pb,Pt}$ 3071 Hz.

In common with the ethene and norbornene systems, the growth of resonances ascribed to (DIOP)Pt $(CN)_2$ were observed after a few minutes at ambient temperature. These resonances dominated the spectrum after two hours, and were the only observable signals after a further 12 hours at 278 K.

A ^{1}H N.M.R. study of the reaction showed the presence of a hydride resonance with the same shift and coupling to Pt and P as was observed in the reaction of (DIOP)Pt norbornene. The hydride resonances were however considerably reduced in intensity relative to the signal observed using identical conditions and concentrations for (DIOP)Pt norbornene. The reduced intensity of the hydride resonance also suggests that the hydridocyanide $\underline{4}$ is not the only product of the reaction, in agreement with the ^{31}P data (see below (iii)).

(iii) <u>With excess reagents</u>. When excess HCN was added to a solution of (DIOP)Pt norbornadiene in the presence of excess norbornadiene at ambient temperature, resonances of species (a) and (b) from 3.3.3.(ii) appeared instantly, and in roughly equal amounts. Smaller resonances due to $\underline{4}$ were present initially,

but these disappeared after about ten minutes to leave the spectrum shown in <u>Figure 7</u>, which contained only species (a) and (b). The spectrum remained unchanged for 2-3 hours before resonances ascribed to $(DIOP)Pt(CN)_2$ began to grow in intensity.

The low value of $^1J_{PPt}$ for (a) suggests that the coordination number of the platinum is high. A σ-alkyl, π-olefin coordinated norbornadiene <u>8</u> seems likely.
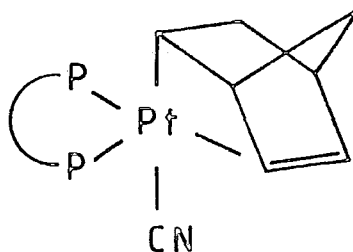
<u>8</u>

σ-alkyl π-olefin complexes of norbornadiene have been observed in systems in which nucleophilic attack of one bound olefin in a diolefin complex has occurred, [2,29]. A σ-alkyl, π-olefin complex intermediate <u>9</u> has been postulated in the palladium catalysed hydrocyanation of 5-vinyl-norbornene to give a tricyclic nitrile, <u>Scheme 7</u>, [30].

The involvement of a species such as <u>8</u> in the catalytic cycle of the hydrocyanation of norbornadiene may provide an explanation for the very different optical yields from the hydrocyanation of norbornadiene and norbornene (7S vs. 10R) [31], as obviously no equivalent to <u>8</u> is possible for norbornene.

The species (b) is more difficult to assign. The two

Figure 7. PHOSPHORUS N.M.R. SPECTRUM OF

DIOP Pt NORBORNADIENE + EXCESS

HCN & NORBORNADIENE.
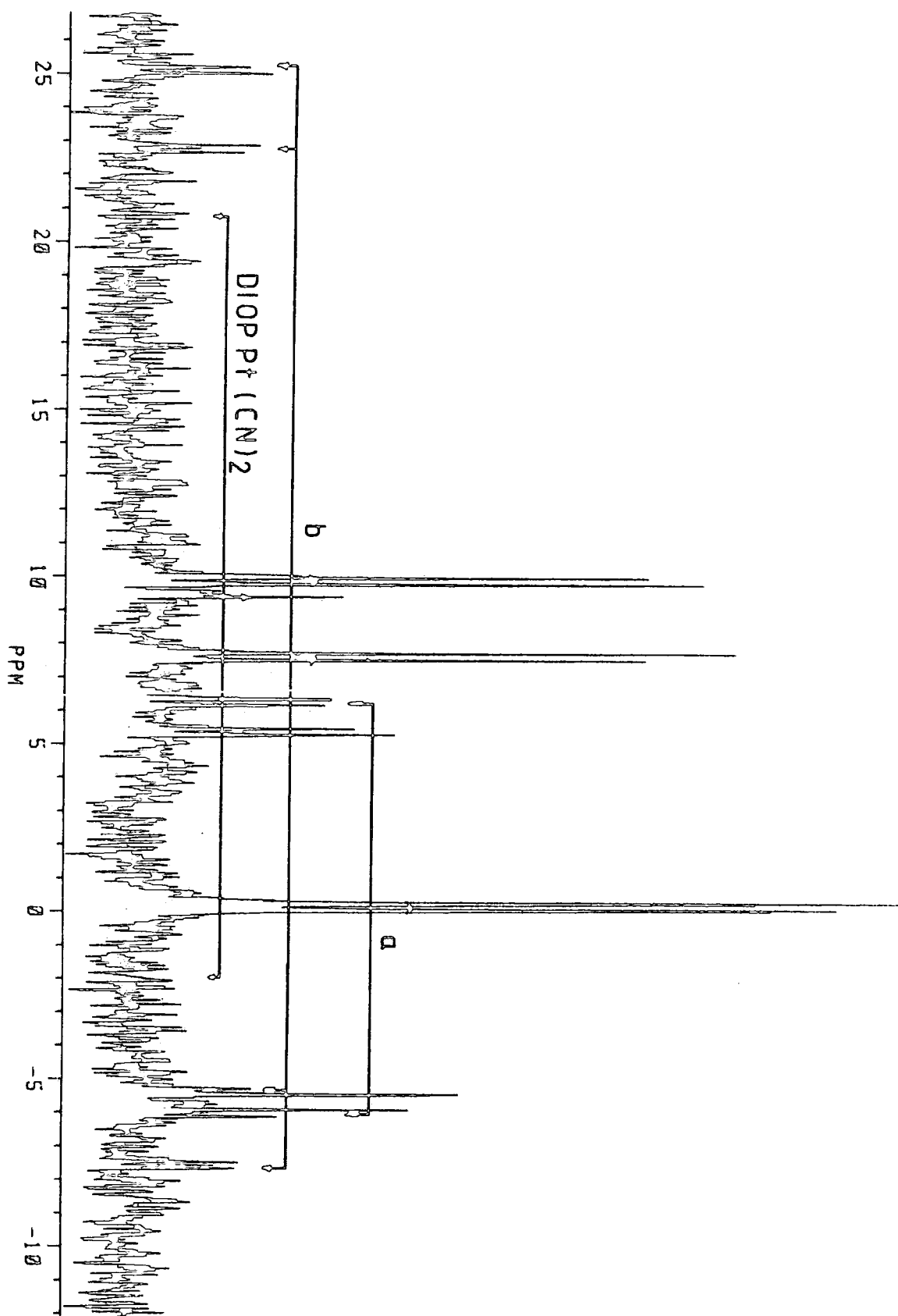
larger values of $^1J_{PPt}$ suggest that both phosphorus atoms are trans to similar ligands in a platinum(II) complex.

$\underline{9}$
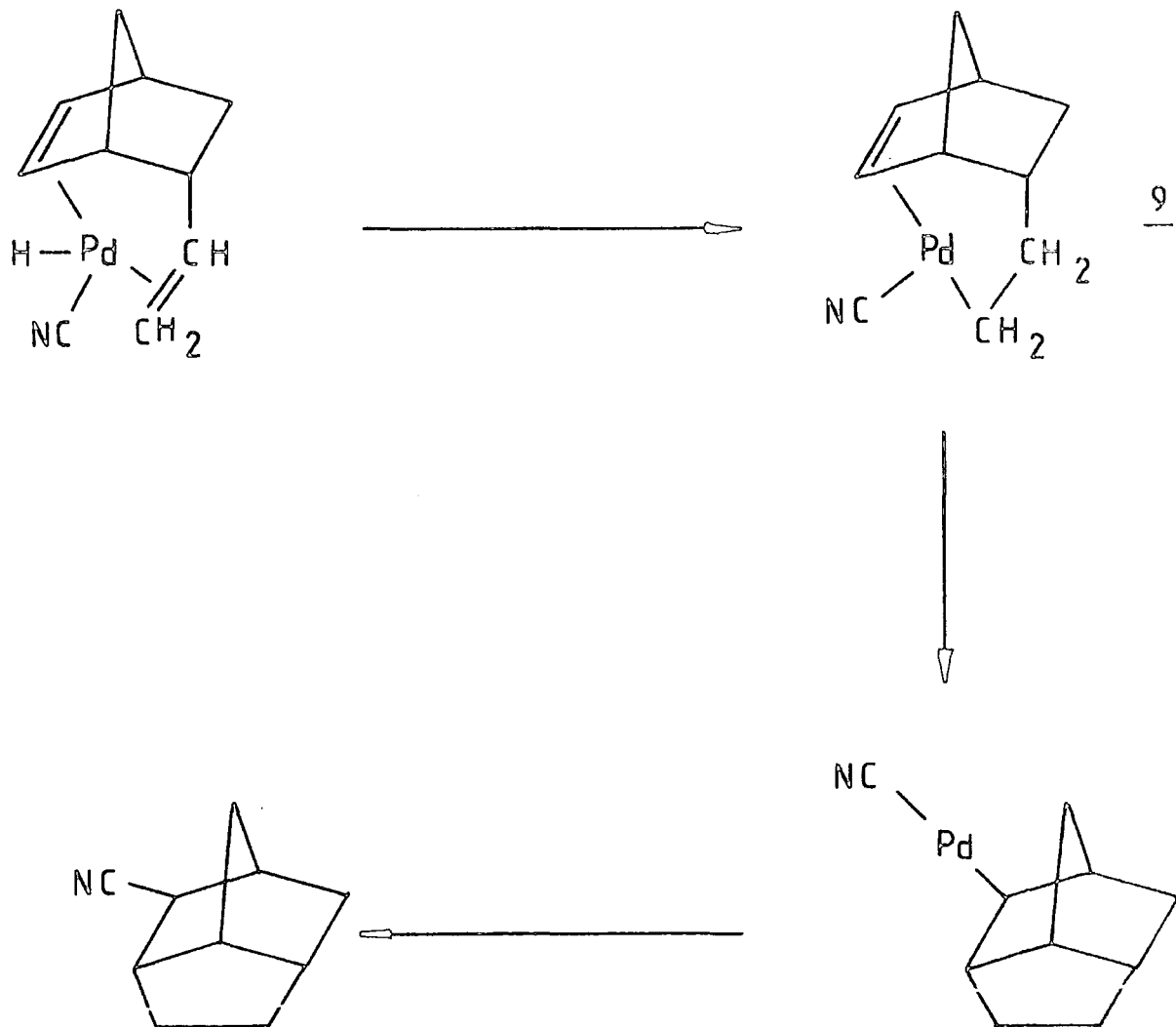
Scheme 7

3.4.   ATTEMPTED REACTIONS OF Pt(DIOP)$_2$

Pt(DIOP)$_2$ was formed as a yellow solution in toluene by addition of one equivalent of DIOP to (DIOP)Pt ethene. The ^{31}P N.M.R. spectrum of the complex at 293 K showed a Pt coupled singlet at $\delta^{31}P$ -10.7 ppm $^1J_{PPt}$ 3764 Hz.

Pt(DIOP)$_2$ failed to show any reaction by ^{31}P N.M.R. (or colour change) with any of the following, norbornene, norbornadiene, hydrogen cyanide, vinylacetate, cis or trans

butenenitrile. This behaviour is predicted considering the
inertness of Pd(DIOP)$_2$ (section 3.2.). A summary of the ^{31}P
N.M.R. spectral parameters of the platinum complexes is
contained in Table 2.

TABLE 2. ^{31}P N.M.R. Data of (DIOP)-Platinum Complexes

Compound	δ_P(ppm)	δ_{Pa}	δ_{Pb}	$^1J_{PaPt}$	$^1J_{PbPt}$	$^2J_{PaPb}$
(DIOP)Pt-ethene	+13.7			3585		
(DIOP)Pt-norbornene	+15.8			3414		
(DIOP)Pt-norbornadiene	+14.6			3251		
(DIOP)Pt(CN)$_2$	+ 9.0			2320		
(DIOP)$_2$Pt	-10.7			3764		
(DIOP)PtHCN		+5.1	+4.1	2840	1725	17

3.5. THE (DIOP) PALLADIUM ETHENE SYSTEM

"Palladium olefin and acetylene complexes are much less
stable than their platinum analogues; few have been prepared
and even fewer isolated" [32]. This applies particularly to the
zerovalent metals [16], but also the metals in their divalent
state [33].

The reactivity of (DIOP)Pt ethene encouraged a search for a
similar palladium system to study. Almost all of the known
palladium(0) alkene complexes are of highly electron poor
alkenes, [34]. The first complexes of an unactivated olefin
were reported in 1971 [35]. They were ethene complexes prepared
by alkylaluminium reduction of bis(acetyl-acetonato)-
palladium(II) in the presence of phosphine and ethene (Scheme 8)
[36].

$$Pd(acac)_2 \quad + \quad 2PR_3 \quad + \quad C_2H_4 \quad + \quad 2AlEt_2(OEt)$$

$$\longrightarrow \quad Pd(C_2H_4)[P(C_6H_5)_3]_2{}^+$$
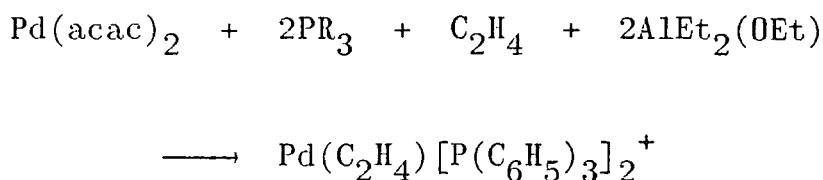
Scheme 8

The use of aluminium alkyls, which are difficult to handle, puts a serious limitation on the use of this preparative method.

Few other palladium(0) ethene complexes have been reported. A more recent paper describes the preparation of $Pd(C_2H_4)$(diphos), and $Pd(C_2H_4)[P(n-Bu)_3]_2$ by U.V. irradiation of $Pd(C_2O_4)$(diphos) or $Pd(C_2O_4)[P(n-Bu)_3]_2$ solutions under ethene. Both of the above preparative methods require relatively specialised apparatus and the complexes were reported to be unstable and impossible to isolate, [32].

3.5.1. The Preparation of (DIOP) Palladium Ethene

The most desirable complex to synthesise for further mechanistic investigations was (DIOP) palladium ethene. It was not documented in the literature, and several attempts to prepare the complex at other laboratories had been unsuccessful, [37].

The first method tested in this study was an adaption of the preparation of (DIOP) platinum ethene [19]. This involved the reduction of (DIOP)PdCl$_2$ with excess sodium borohydride in a mixture of dichloromethane and ethanol.

$$(DIOP)PdCl_2 \quad + \quad C_2H_4 \quad \longrightarrow \quad (DIOP)Pd(C_2H_4) \quad + \quad 2Cl^-$$

10
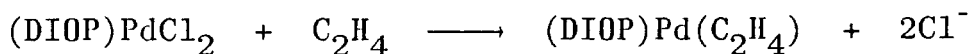
The reduction was carried out with a strong flow of ethene gas through the solution, which was initially cooled to $-78^{0}C$ and was allowed to warm to room temperature gradually. Crystals began to appear after about half an hour at ambient temperature but they began to darken and decomposed during isolation. Several subsequent attempts at the preparation simply produced colloidal palladium metal. Hydrazine hydrate was substituted for the borohydride, also without success. Finally the experiment was carried out with a smaller excess of sodium borohydride, when the reaction yielded colourless monoclinic crystals of (DIOP)Pd ethene 10 in about 70% yield.

3.5.2. The Crystal Structure of (DIOP) Palladium Ethene

The reasonably air stable crystals of the complex were analysed by X-ray crystallography, yielding the first reported structure of a palladium ethene complex. The ORTEP diagram of the structure is shown in **Figure 8**. The bond length and bond angle data are contained in Tables 3 and 4.

Many olefin complexes of the nickel triad containing the metal in the zerovalent state are complexes with electron poor alkenes. Most of the published crystal structures are of such electron-poor alkene complexes, [34], although the structures of the ethene complexes $(PPh_3)_2M(C_2H_4)$ for Ni and Pt are known, [38,39].

Features common to all known structures are:

(i)   the olefinic C=C bond is lengthened on coordination:

(ii) In phosphine complexes the MCC plane is the same as, or is at a small ($\sim 10^{0}$) angle to the MPP plane, i.e. there is a trigonal coordination geometry about the metal.

(iii) The substituents on the alkene are bent away from the metal.

Figure 8. Crystal Structure of DIOP Pd Ethene.

X-ray Crystal Structure was determined by George Ferguson,
University of Guelph, Canada.

(iv)   Coordination is symmetrical.

The structure of (DIOP) palladium ethene shows all of the above characteristics. Rationalisation of the features observed is provided well by the Dewar-Chatt model of olefin binding, in terms of σ donation from the filled olefin π orbital into empty metal orbitals, coupled with π donation from the metal into the π^* LUMO of the alkene, [2,33,34]. Zerovalent complexes of the nickel triad have a d^{10} configuration and are normally tetrahedral. The 16 electron olefin complexes of the metals exhibit trigonal coordination geometry, with the alkene lying in the same plane as the phosphine ligands. This is in contrast to M(II) d^8 olefin complexes, where the olefin adopts a sterically more favourable orientation, perpendicular to the ligand plane.

The confinement of the olefin to the ligand plane in the 16 electron d^{10} complexes may be due to the greater stabilization afforded by π donation of electron density from the higher energy, more antibonding molecular orbital, which resembles the metal d_{xz} orbital (coordinates as in Figure 9) [40], compared with the lower energy orbital resembling the metal d_{yz} orbital, which may already be involved in π back donation to the phosphine ligands. Olefins are generally poor σ donors, and
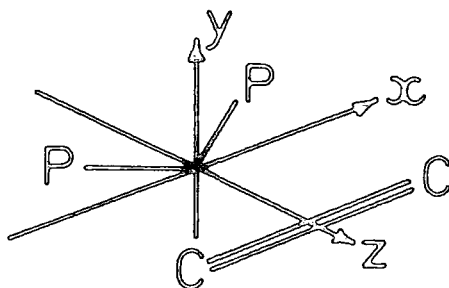
Figure 9

TABLE 3. Bond lengths in 6b ($\overset{\circ}{A}$)[a]

Pd	P1	2.289(2)	C12	C13	1.387(14)
Pd	P2	2.289(2)	C13	C14	1.345(14)
Pd	C1	2.122(9)	C14	C15	1.317(13)
Pd	C2	2.119(8)	C15	C16	1.386(13)
P1	C3	1.840(8)	C21	C22	1.367(11)
P1	C11	1.831(8)	C21	C26	1.380(10)
P1	C21	1.828(5)	C22	C23	1.392(9)
P2	C6	1.843(7)	C23	C24	1.349(14)
P2	C31	1.828(5)	C24	C25	1.369(14)
P2	C41	1.834(7)	C25	C26	1.404(10)
O1	C4	1.407(9)	C31	C32	1.386(9)
O1	C7	1.423(9)	C31	C36	1.379(10)
O2	C5	1.407(9)	C32	C33	1.381(12)
O2	C7	1.402(10)	C33	C34	1.368(14)
C1	C2	1.366(11)	C34	C35	1.332(12)
C3	C4	1.528(10)	C35	C36	1.399(10)
C4	C5	1.529(8)	C41	C42	1.376(12)
C5	C6	1.511(9)	C41	C46	1.366(12)
C7	C8	1.502(11)	C42	C43	1.372(13)
C7	C9	1.480(13)	C43	C44	1.377(16)
C11	C12	1.369(11)	C44	C45	1.301(19)
C11	C16	1.378(11)	C45	C46	1.396(13)

a) Estimated standard deviations are given in parentheses.

TABLE 4. Bond Angles (Degrees)[a]

P1	Pd	P2	106.41(7)	O1	C4	C3	108.6(6)
P1	Pd	C1	145.2(2)	O1	C4	C5	102.2(5)
P1	Pd	C2	108.0(2)	C3	C4	C5	118.6(5)
P2	Pd	C1	108.1(2)	O2	C5	C4	102.1(5)
P2	Pd	C2	145.6(2)	O2	C5	C6	106.3(6)
C1	Pd	C2	37.6(3)	C4	C5	C6	118.9(5)
Pd	P1	C3	117.0(2)	P2	C6	C5	114.9(5)
Pd	P1	C11	111.6(2)	O1	C7	O2	105.3(6)
Pd	P1	C21	120.5(3)	O1	C7	C8	109.5(5)
C3	P1	C11	103.6(3)	O1	C7	C9	109.6(8)
C3	P1	C21	100.3(3)	O2	C7	C8	108.2(8)
C11	P1	C21	101.3(3)	O2	C7	C9	110.9(6)
Pd	P2	C6	115.0(2)	C8	C7	C9	113.1(9)
Pd	P2	C31	117.8(2)	P1	C11	C12	125.0(6)
Pd	P2	C41	116.9(2)	P1	C11	C16	116.9(6)
C6	P2	C31	100.5(3)	C12	C11	C16	118.0(8)
C6	P2	C41	102.1(3)	C11	C12	C13	119.8(8)
C31	P2	C41	101.9(3)	C12	C13	C14	120.9(8)
C4	O1	C7	110.3(6)	C13	C14	C15	120.1(9)
C5	O2	C7	107.1(5)	C14	C15	C16	121.0(8)
Pd	C1	C2	71.1(5)	C11	C16	C15	120.2(8)
Pd	C2	C1	71.3(5)	P1	C21	C22	122.4(5)
P1	C	C4	112.4(5)	P1	C21	C26	1 3(5)

TABLE 4 cont.

C22	C21	C26	119.3(6)
C21	C22	C23	120.4(8)
C22	C23	C24	121.0(9)
C23	C24	C25	119.3(7)
C24	C25	C26	120.8(8)
C21	C26	C25	119.1(7)
P2	C31	C32	121.6(6)
P2	C31	C36	120.0(5)
C32	C31	C36	118.2(7)
C31	C32	C33	120.4(9)
C32	C33	C34	121.1(8)
C33	C34	C35	118.7(7)
C34	C35	C36	122.3(8)
C31	C36	C35	119.4(7)
P2	C41	C42	117.0(6)
P2	C41	C46	124.9(6)
C42	C41	C46	118.1(7)
C41	C42	C43	121.8(9)
C42	C43	C44	119.1(10)
C43	C44	C45	118.9(9)
C44	C45	C46	123.8(11)
C41	C46	C45	118.2(9)

a) Estimated standard deviations are given in parentheses.

good π acceptors. In the extreme case, with very little σ donation and strong π back donation in a complex, there will be a net electron pair transfer to the olefin from the metal, leaving the central metal in the d^8 configuration, which adopts the square planar geometry, bringing the olefin into the ligand plane. The extent of distortion from tetrahedral to 'planar' geometry will depend on the amount of electron density transferred from the metal [33].

The lengthening of the olefinic C=C bond will arise either by loss of bonding electron density in donation from the olefin π bonding orbital to a vacant σ orbital on the metal, or the gain of antibonding electron density in the olefin π^* antibonding orbital by π donation from the metal.

Palladium is considered to have the least aptitude to form $d\pi$ bonds compared with the other two metals in the nickel triad in the d^{10} state. This unwillingness to release electron density is reflected in the (n-1)d $\rightarrow$ n(p) promotion energies for the triad of 1.72, 3.28 and 4.23 eV for Ni, Pt and Pd respectively, [41].

Ethene is a better π donor and a poorer π acceptor than olefins with electron withdrawing substituents, so it is not surprising that the C-C bond length in (DIOP) palladium ethene is 1.366(11)Å, which is only 0.03Å longer than the 1.337(2)Å of free ethene. The complexes $(PPh_3)_2M(C_2H_4)$ have C-C bond lengths of 1.46Å for M = Ni [38] and 1.43Å for M = Pt [39]. Although the short C-C bond length in (DIOP) palladium ethene suggests less disruption of the alkene double bond than in related d^{10} 16 electron complexes, the position of the C-C bond axis is almost

in the ligand plane, $\alpha = 5.8^\circ$ (Figure 10).
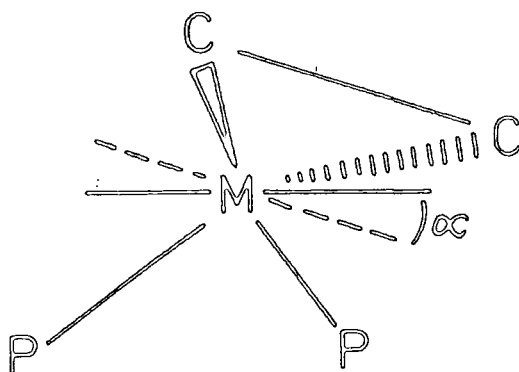
Figure 10.

This suggests that the bonding is similar to that in other olefin complexes, with π back donation into the olefin π^* orbitals being sufficiently important to confine the olefin to the ligand plane.

The palladium-carbon bonds are 2.12Å and are equal in length. This compares with 2.00Å for $(PPh_3)_2NiC_2H_4$ and 2.11Å for $(PPh_3)_2PtC_2H_4$. The C(1)Pd C(2) angle of 37.6° is acute in comparison to $(PPh_3)_2NiC_2H_4$ (42.1°) and is less than the C(1)Pt C(2) angle found in a range of $(PPh_3)_2Pt$ olefin complexes of 40.6 to 47.1° [34]. This small angle presumably reflects the fact that although the olefin is at a similar distance from the metal, the C-C bond length is shorter in (DIOP) palladium ethene.

The chelate bite angle in (DIOP) palladium ethene is $106.41(7)^\circ$, compared with 96° in the square planar d^8 complex DIOP $PdCl_2$, [42]. The more obtuse angle in the ethene complex may be due to the greater steric requirements of the two chloride ligands. The P, Pt, P bond angle in $(PPh_3)_2Pt$ TCNE is

101°, [43]. The geometry in the TCNE complex would be expected to be more distorted towards a square planar structure, and thus have a smaller P(1)Pt P(2) angle, since TCNE is a much better π acceptor than ethene.

3.5.3. The Stability of (DIOP) Palladium Ethene

Crystals of (DIOP)Pd ethene may be stored in an atmosphere of ethene at 5^OC for weeks without deterioration. However some loss of ethene was noted after several months under such conditions. The crystallographer noted there was no loss of reflection intensity on 3 representative reflections which were checked every four hours whilst the X-ray data was collected at 23^OC, indicating reasonable stability.

Solutions of the complex in methylene chloride or benzene began to turn orange-red after a few minutes at room temperature. Palladium metal was deposited from such solutions after several hours. Exposure of solutions of the complex to air accelerated the formation of colouration. ^{31}P N.M.R. spectra showed loss of the single resonance at δ +6.8 from the complex, and the appearance of a signal at δ_p +27 ppm which was eventually the only peak in the spectrum. The δ 27 ppm resonance was ascribed to DIOP oxide, and the assignment was confirmed by addition of DIOP oxide to the solution, which increased the intensity of the peak in question.

Under an ethene atmosphere the decomposition was considerably decreased, solutions remaining colourless for up to an hour at room temperature. The absence of a ^{31}P N.M.R. resonance at δ^{31}P -1.2 ppm, together with no detectable free ethene in the ^{1}H N.M.R. spectrum of 10 (Figure 11), indicate

Figure 11. PROTON N.M.R. SPECTRUM OF DIOP PALLADIUM ETHENE.
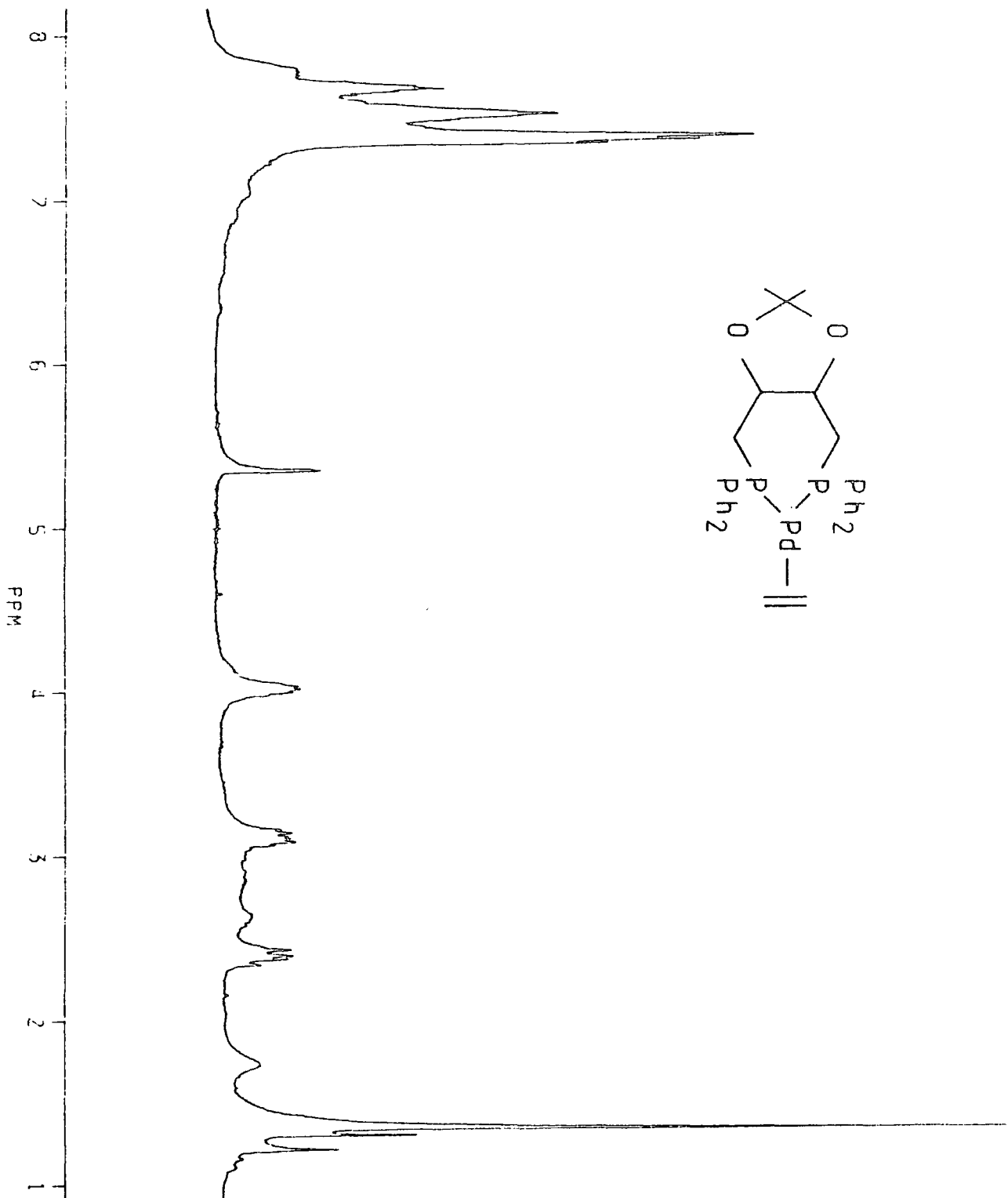
that the complex is stable to dissociation and
disproportionation, which occurs for some other palladium ethene
complexes in solution [35], Scheme 9.

$$(DIOP)PdC_2H_4 \xrightleftharpoons{K_1} (DIOP)Pd + C_2H_4$$

$$2(DIOP)Pd \longrightarrow (DIOP)_2Pd + Pd$$
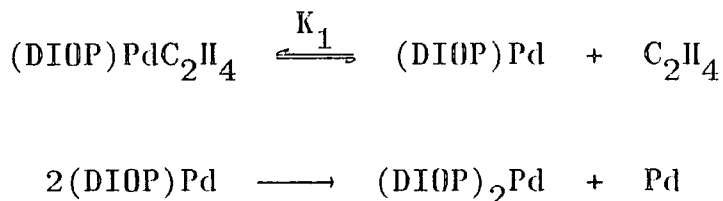
Scheme 9

An upper limit of $K_1 = 2 \times 10^{-6}$ M may be set by assuming
that 2×10^{-4} M of free ethene could be detected in a 0.02 M
solution of 10.

Fourteen electron complexes of the type ML_2 (L =
monodentate phosphine or $\frac{1}{2}$ bidentate phosphine) are highly
reactive, especially when approach to the metal centre is
unhindered, as would be the case for (DIOP)Pd. PtL_2 species
with monodentate phosphines have been implicated as
intermediates in reactions of L_2Pt olefin complexes [44]. The
complex $(PPh_3)_2Pd$ has been assumed to be the actual catalyst
undergoing oxidative addition in reactions with organic halides,
[45].

Unlike some other palladium ethene complexes, which lose
ethene to give L_2Pd species at reduced pressure, [35], 10 shows
no change in its ^{31}P or [1]H N.M.R. spectrum after the solid has

been at 0.01 mmHg for 15 minutes; or if a solution is evaporated to dryness then the solid redissolved.

It is possible, even with a small value of K_1, that the 14 electron (DIOP)Pd fragment is present in sufficient concentrations to react with oxygen, initiating decomposition of the complex, leading finally to DIOP oxide and metallic palladium; and that an ethene atmosphere suppresses this dissociation. Alternatively reaction with O_2 may occur associatively as indicated in <u>Scheme 10</u>. This route seems more likely as dissociative exchange of alkene is clearly not occurring.
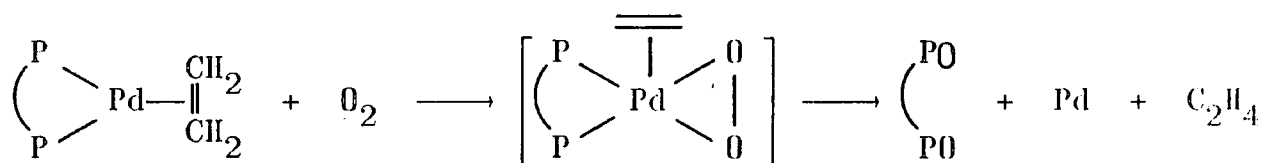
<u>Scheme 10</u>

Tolman found no detectable dissociation in solutions of $C_2H_4ML_2$ complexes for M = Ni, Pd, Pt, (L = various PR_3 ligands) [16].

Bound ethene resonances of <u>10</u> appear at δ^1H 2.59 and 2.36. analogous to the bound ethene resonances of (DIOP)Pt ethene at δ 1.0 and δ 2.0 ppm due to two pairs of trans related diastereotopic olefin protons. Ittel and Ibers noted a

correlation between the chemical shift of bound olefinic protons and the length of the complexed C=C bond in a series of olefin ML_2 complexes [M = Ni, Pt, L = phosphines], [46]. They suggest that increased shielding of olefinic protons occurs as more electron density is transferred from the metal to the ligand, shifting [1]H N.M.R. resonances to higher frequency, and that this can be correlated with the C=C bond lengths obtained from X-ray crystallographic data. The ^{1}H resonances of the ethene protons in 10 are to higher frequency than predicted by the correlation in reference 46. For a C=C bond length of 1.366(11)Å, the resonances would be expected at 5.5 ppm rather than around 2.5 ppm as actually observed. This highlights the danger of attempting to draw too much information from chemical shift data alone. X-ray crystallographic studies are carried out on a solid, whereas the N.M.R. spectra are obtained in solution. It is perhaps worth noting however that the ethene proton resonances in (DIOP)Pt ethene are to higher frequency than those of (DIOP)Pd ethene, consistent with the model described above, i.e. with more electron density transferred from platinum than palladium to ethene, causing greater shielding of the ethene protons when M = Pt.

3.5.4. Reactions of DIOP Palladium Ethene

(i) With added phosphine. When one equivalent of free DIOP is added to a solution of 10, zerovalent $(DIOP)_2Pd$ is formed quantitatively, as evidenced by the loss of the δ_P +6.8 resonance from the [31]P N.M.R. spectrum for a single sharp peak at δ -1.2 ppm. Further additions of DIOP leave the δ -1.2 peak unchanged and a new sharp peak appears at δ -22 ppm due to free

DIOP.

(ii) <u>With alkenes</u>. Addition of ethene to solutions of <u>10</u> leads to an exchange broadened ^{1}H signal for free ethene centred at 5.2 ppm. The broad resonance sharpens upon addition of more ethene ($\omega_{\frac{1}{2}}$ = 20 Hz with an approximately 40 M excess of ethene in CD_2Cl_2). The resonances due to bound ethene were too broad to observe. A solution of <u>10</u> which had partly decomposed gave broad ethene resonances (δ 5.2) due to exchange of intact <u>10</u> with ethene liberated during decomposition. The mechanism of exchange is presumably therefore <u>associative</u>, with a very low formation constant for the intermediate associated complex, as no direct evidence for the existence of a bis olefin complex was found.

Displacement of ethene by other alkenes was monitored by [31]P N.M.R. spectroscopy. DIOP Pd ethene has a single sharp resonance in its [31]P N.M.R. spectrum at δ_P +6.8 ppm in CD_2Cl_2. Addition of three equivalents of norbornene broadened the resonance due to (DIOP)Pd ethene and produced a new, broad resonance $\omega_{\frac{1}{2}} \sim$ 70 Hz at $\delta^{31}P$ +6.2 ppm. Addition of a further twenty equivalents of norbornene left a single sharp resonance at δ 6.2, ascribed to the alkene complex DIOP palladium norbornene <u>11</u>. The broad signals at the lower concentration of norbornene indicate that an exchange process is occurring, <u>Scheme 11</u>.
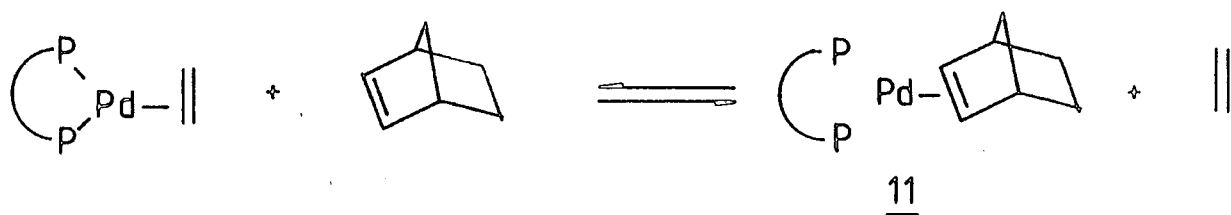
Scheme 11

Tolman showed [15] that the relative stabilities of olefin complexes of the type olefin $Ni[P(o-o-tolyl)_3]_2$ were governed by the electronic properties of the olefin, and found a linear relationship between the energy of the olefin LUMO, (determined by examining ionization potential and u.v. data for various olefins) and log K_1, the formation constant for the complex. He noted that the sensitivity of nickel to the energy level of the olefin LUMO would be higher than the sensitivity of Pt(0), Rh(I) etc., as the metal HOMO energy decreases $Ni(0) > Fe(0) > Pt(0) > Rh(I)$: the lower energy metal HOMO having a poorer energy match with the higher energy olefin LUMO. In this way the selectivity of the metal for different olefins is expected to decrease. Palladium(0) has a lower HOMO than both Pt(0) and Ni(0), and should therefore have the lowest selectivity towards different olefins.[†] This may explain the need for an excess of norbornene to displace the ethene from (DIOP)Pd ethene. However 10 did not appear to react (by ^{31}P N.M.R.) with either a 100 M excess of cyclopentene, cyclohexene, or vinyl acetate. Enantiomerically pure (-)-carvone 12 is bound regioselectivity by the conjugated alkene and stereoselectively by the Si-Si face so that only one diastereomer is observed.

[†] Tolman used the 1st ionization potentials of 7.6 eV for Ni, 8.3 eV for Pd and 9.0 eV for Pt, as the level of the metal HOMO's. The olefin LUMO energies vary from 3 to 5.5 eV. The spin paired 1st ionization potentials are 5.8 eV for Ni, 8.3 eV for Pd and 8.2 eV for Pt. Using these values, the selectivity of nickel is greater, and palladium, rather than platinum would be expected to have the lowest selectivity.

12
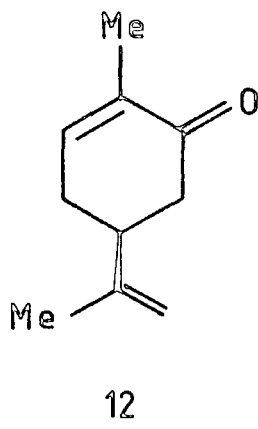
'   One equivalent of TCNE added to a solution of 10 quantitatively produced the (DIOP)Pd TCNE species with δ_P +8.8 ppm which was obtained independently by addition of TCNE to DIOP$_2$Pd (section 3.2.2.).

(iii) **With HCN**. Reaction of 10 with ~ 20 equivalents of HCN in CD$_2$Cl$_2$ gave a pale yellow/green solution, which rapidly faded to a homogeneous clear solution. The ^{31}P N.M.R. of such solutions, when prepared carefully under argon, contained resonances ascribed as follows: Initially the resonance of 10 vanished and was replaced by a species 13 δ_{Pa} +4.0 ppm δ_{Pb} -6.3, J_{PaPb} 13 Hz and a singlet 14 δ_P 17.6 ppm. The resonance of 14 was small to begin with, but became the dominant peak in the spectrum after two hours. The growth of this signal was accelerated by higher HCN concentrations. The resonance is thus most probably due to the dicyanide, as depicted in <u>Scheme 12</u>. ^{1}H spectra of the reaction solution show the appearance of free ethene with δ^1H 5.25 ppm, as well as a broad hydride resonance at δ -4.9, which broadens further on addition of more HCN. This evidence suggests that 13 is a hydridocyanide analogous to that formed by platinum (section 3.3.1.). When HCN addition is carried out
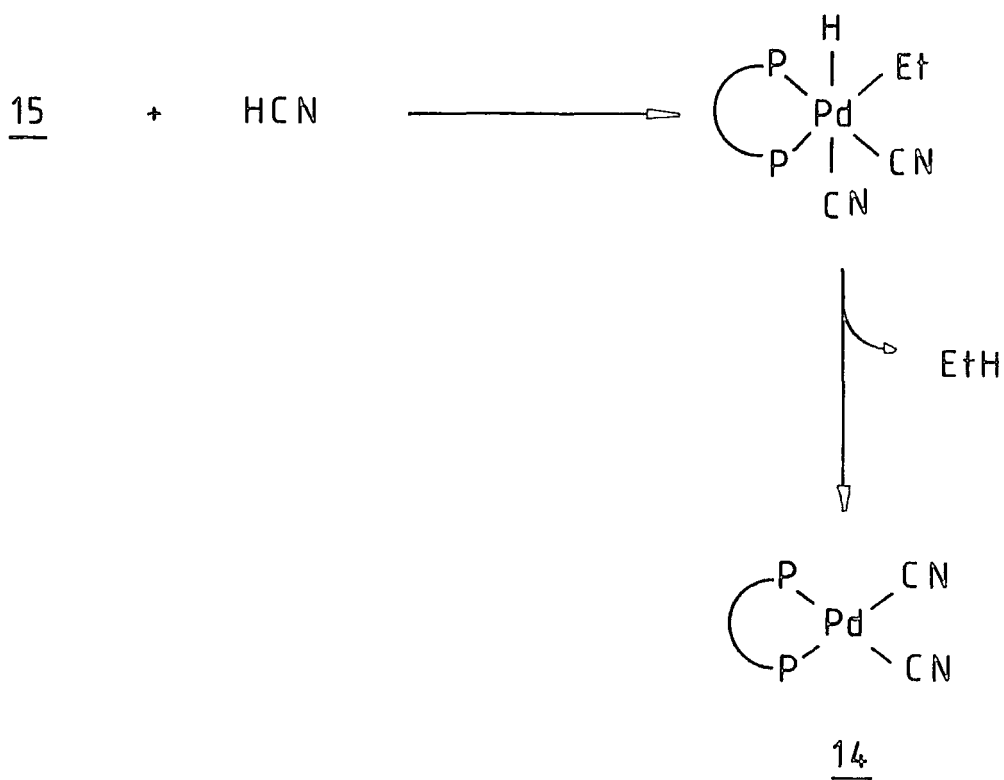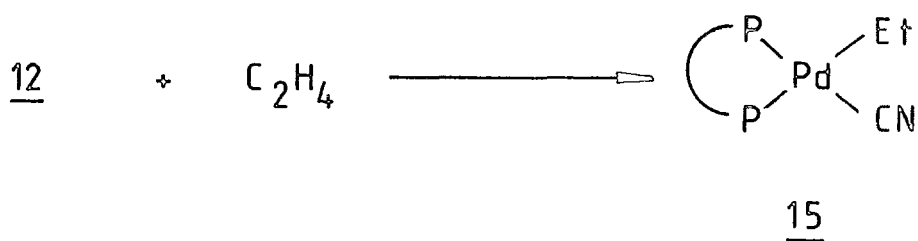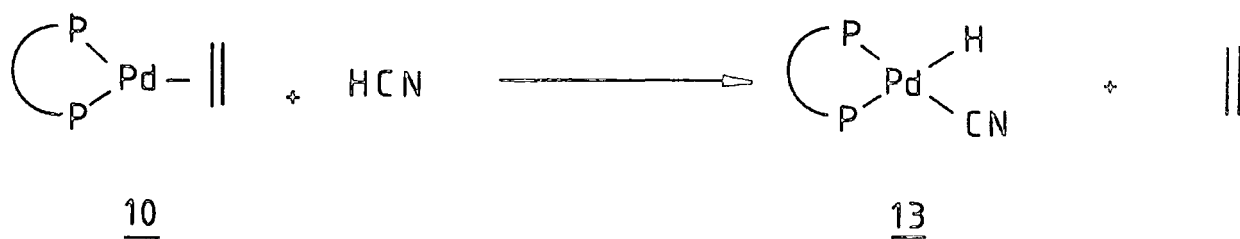
Scheme 12

under an ethene atmosphere, a further species 15 is observed, with δ^{31}Pa +18.2, δ_{Pb} -1.4 ppm J_{PaPb} 40 Hz (Figure 12).

(DIOP)Pd norbornene reacts with HCN to give 13 and 14 only, even when a 50-fold excess of norbornene is present in the solution. Tolman has shown that ethene forms observable nickel ethylcyanide complexes with phosphite ligands, whereas other alkenes do not, [6]. A plausible structure for 15 therefore is a palladium ethylcyanide species. Although this could form by direct oxidative addition to 10 it seems more likely from the experimental data described above that ethene is initially displaced and that 15 forms by reaction of 13 with excess ethene.

With the other alkenes and with analogous platinum complexes, reaction of the hydridocyanide (DIOP)M(H)CN with added alkene to give observable species did not occur, and competitive formation of DIOP M(CN)$_2$ took place, presumably as shown in Scheme 13.

(v) With nitriles. (DIOP)Pd ethene showed no reaction with acetonitrile, benzonitrile or norbornane carbonitrile, either in stoichiometric amounts or in excess.

(vi) Other oxidative addition reactions. Allyl acetate reacts rapidly with (DIOP)Pd ethene, to give a species with a singlet in the ^{31}P spectrum at δ^{31}P of 8.1 ppm, assigned to the cationic η^3 allyl complex 16 (Scheme 14). This simple reaction is of direct relevance to the mechanism of the palladium catalysed asymmetric alkylation of allyl substrates [47].

Figure 12. PHOSPHORUS N.M.R. SPECTRUM OF DIOP Pd ETHENE + HCN + EXCESS ETHENE.
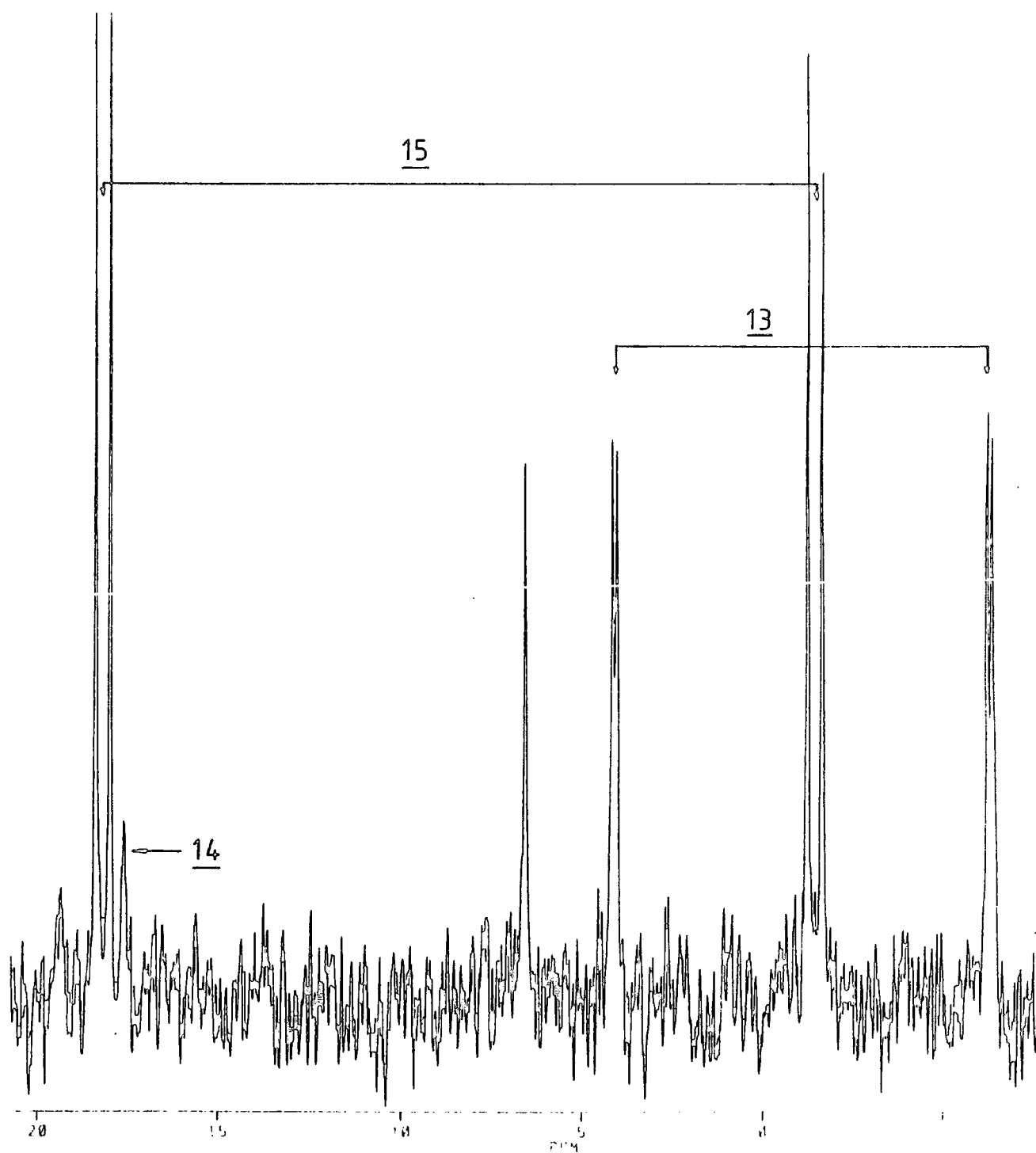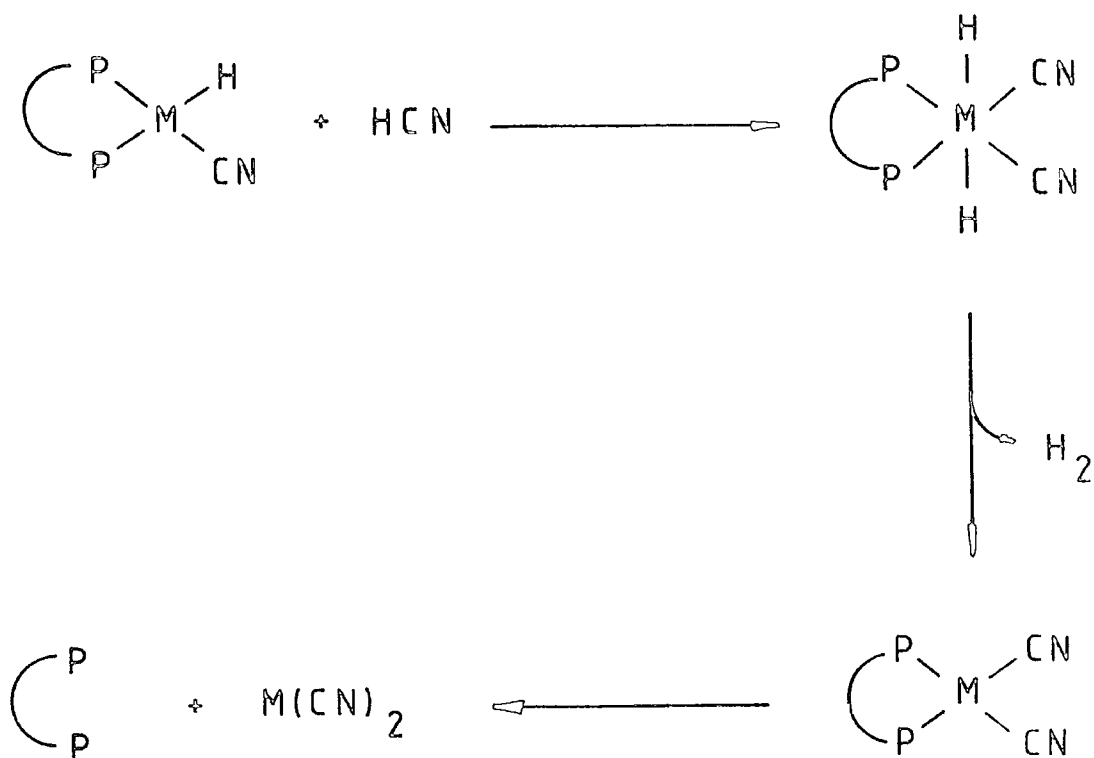
Scheme 13
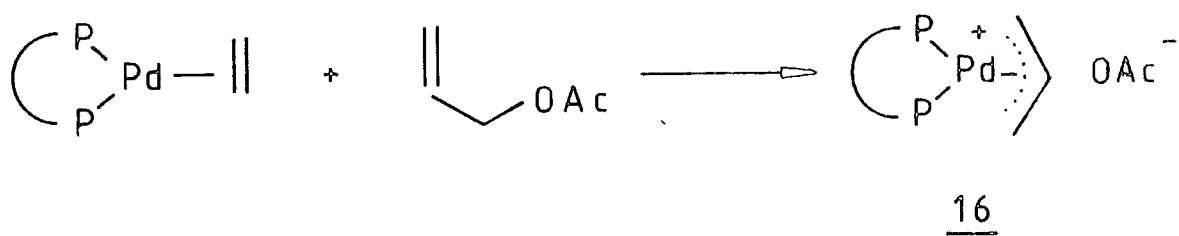
Scheme 14

(DIOP)Pd ethene reacts with $CHCl_3$, $CDCl_3$ or CCl_4 to give (DIOP)PdCl$_2$, the presence of which is seen in the [31]P N.M.R. spectrum. When $CHCl_3$, $CDCl_3$ or CCl_4 was added to a solution of (DIOP)Pd ethene in CD_2Cl_2, the resonance of (DIOP)Pd ethene vanished and was replaced by a singlet at $\delta^{13}P$ +16 ppm, the intensity of which was increased by the addition of an authentic sample of (DIOP)PdCl$_2$. These reactions probably occur by direct halogen atom abstraction to give a 15 electron [(DIOP)-Pd-X] radical intermediate. Similar single electron transfer mechanisms have been shown to operate in other d^{10} [48-50] and d^8 [51] systems.

Osborn and Kramer showed that the reaction of some alkyl halides with $Pd(PEt_3)_3$ and $Pt(PEt_3)_3$ involved one electron processes, for example, they observed CIDNP effects in the [1]H N.M.R. spectra of the products from the reaction of isopropyl iodide with $Pd(PEt_3)_3$, [48].

Tsou and Kochi examined the oxidative addition of aromatic halides to nickel(0) complexes. The presence of paramagnetic nickel(I) species was detected by E.S.R. spectroscopy, [49].

A stable Pd(I) radical was isolated after electrochemical reduction of η^5 $C_5Ph_5Pd(II)^+$(dibenzocyclooctatetraene). The radical η^5 C_5Ph_5Pd (norbornadiene) can be generated, and when reacted with per-benzoic acid gave the σ, π complex 17. 17 was also formed by the reaction of Pd(II)(norbornadiene) with benzoate, Scheme 15.

When allyl chloride was allowed to react with (DIOP)Pd ethene, the products, identified by [31]P N.M.R. were the η^1-allyl

$$C_5Ph_5Pd(nbd) \quad + \quad PhC \overset{\displaystyle O}{\underset{\displaystyle O-OH}{\diagdown}} \qquad \overset{I}{}$$

$$C_5Ph_5Pd(nbd) \quad + \quad PhC \overset{\displaystyle O}{\underset{\displaystyle O^-}{\diagdown}} \qquad \overset{II}{}$$
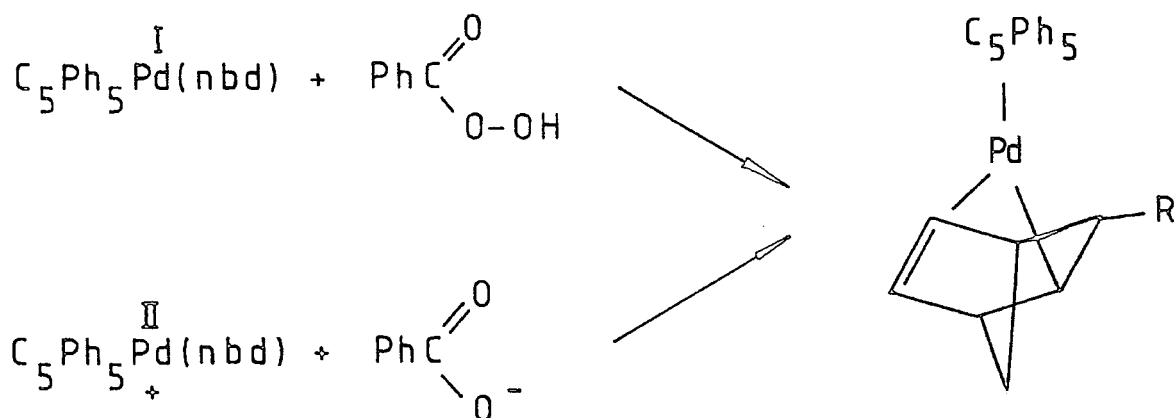
Scheme 15

halide

$$\delta_{Pa} \quad +20.8 \text{ ppm}$$

$$J_{PaPb} \quad 40 \text{ Hz}$$

$$\delta_{Pb} \quad + 2.0 \text{ ppm}$$

and $(DIOP)PdCl_2$, (Figure 13). When the reaction was carried out in the presence of 5 mol % duroquinone, only the η^1-allyl complex was formed. These results indicate that allyl chloride probably reacts by a single electron transfer mechanism. The formation of $(DIOP)Pd(\eta^1$-allyl$)Cl$ in the presence of duroquinone can be explained by collapse of the radical cage pair, or by a competing S_N2 mechanism. The inhibition of the creation of DIOP $PdCl_2$ by duroquinone implies that it is formed by a radical chain mechanism, and that there is competition between halogen abstraction by $[(DIOP)PdCl]\cdot$ and reaction with further allyl chloride to form a σ bond.

Aryl halides readily add oxidatively to palladium(0) complexes. A study of the relative reactivities of various aryl halides towards $Pd(PPh_3)_4$ showed that the reactivity of the halide was related to the order of their reduction potentials,

Figure 13. PHOSPHORUS N.M.R. SPECTRUM OF
DIOP PALLADIUM ETHENE +
ALLYL CHLORIDE.

Pa   20·8 ppm
Pb   2·0 ppm
J_{PaPb} 4·0 Hz

DIOP Pd Cl 2

suggesting that a one electron transfer mechanism may be involved, [53]. Phenyl iodide was found to be the most reactive aryl halide [54]. Reaction of PhI with (DIOP)Pd ethene gave a σ-aryl halide complex whose ^{31}P N.M.R. spectral parameters were (Figure 14).

$$\delta^{31}P \quad \delta_{Pa} \ 13.2 \ ppm$$
$$J_{PaPb} \ 41 \ Hz$$
$$\delta_{Pb} \ -3.2 \ ppm$$

The formation of the aryl halide complex probably also involves a one electron transfer mechanism before covalent bond formation. Such complexes are plausible intermediates in palladium catalysed aryl cross coupling reactions, [45,49].

The reactions of (DIOP)Pd ethene are summarised in Scheme 16. The ^{31}P N.M.R. spectral parameters are summarised in Table 5.

TABLE 5. ^{31}P N.M.R. Data of (DIOP)-palladium Complexes

Compound	δ_P (ppm)	δ_{Pa}	δ_{Pb}	$^2J_{PaPb}$ (Hz)
(DIOP)Pd-Ethene	+ 6.8			
(DIOP)$_2$Pd	- 1.21			
(DIOP)PdCl$_2$	+16.1			
(DIOP)Pd-norbornene	+ 6.2			
[(DIOP)Pd-η^3-allyl]$^+$OAc$^-$	+ 8.1			
(DIOP)Pd-TCNE	+ 9.2			
(DIOP)Pd(CN)$_2$	+17.6			
(DIOP)$_2$Pd	- 1.2			
(DIOP)Pd-(η^1-allyl)Cl		+20.8	+2.0	40
(DIOP)Pd-(η^1-Ph)I		+13.2	-3.2	41
(DIOP)PdHCN		+ 4.0	-6.3	13
(DIOP)Pd(Et)CN		+18.2	-1.4	40
(DIOP)Pd-(-carvone)		+ 7.3	+4.3	47

Figure 14. PHOSPHORUS NMR SPECTRUM OF DIOP PALLADIUM ETHENE + PHENYL IODIDE.

Pa   13·2 ppm

Pb   -3·2 ppm

J_{PaPb} 41 Hz

10

Scheme 16

Reactions of DIOP Pd Ethene
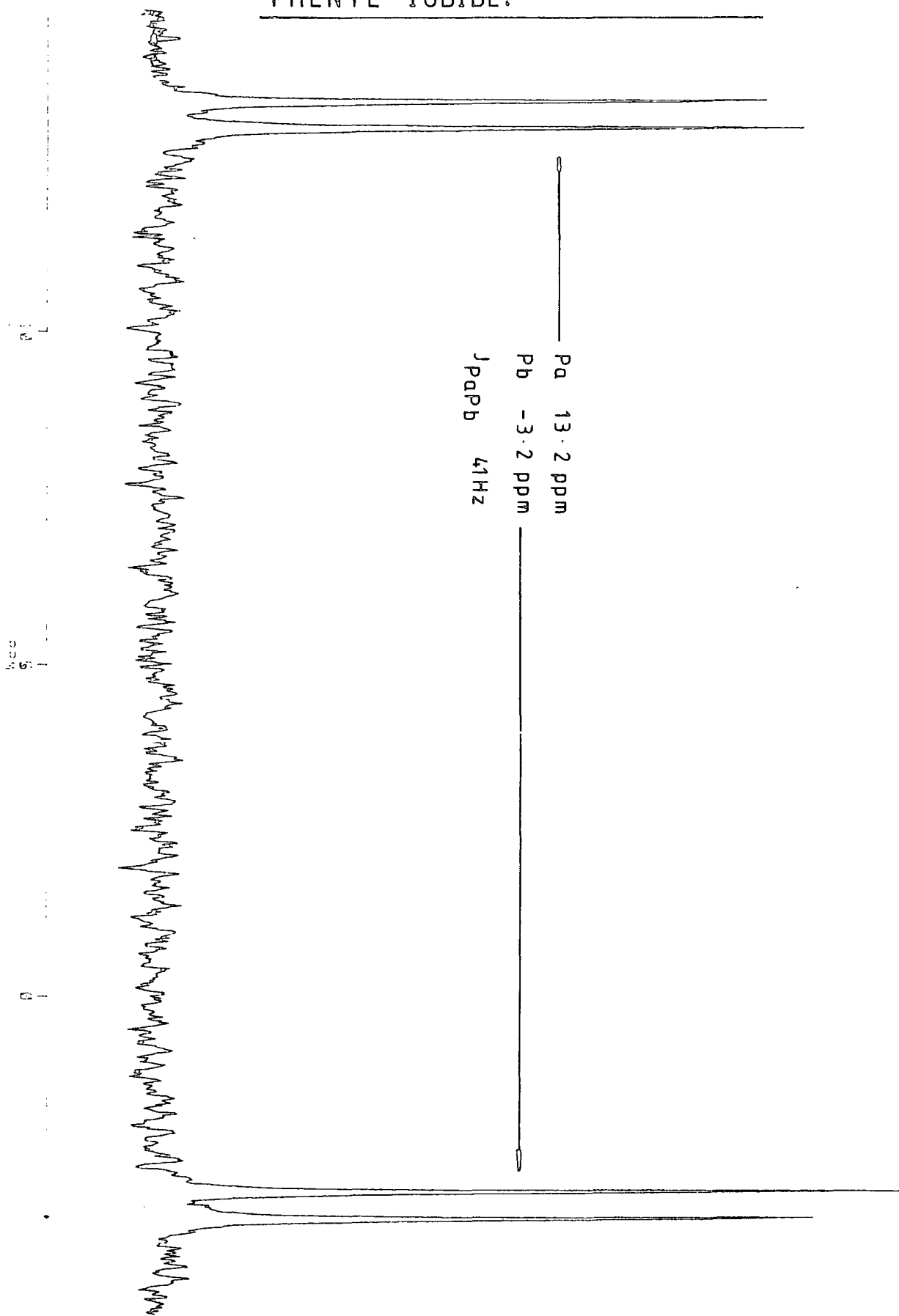
3.5.5. Summary and Mechanistic Proposals

Pd(DIOP)$_2$ is the only observable complex present under ambient conditions in solutions containing the components of the catalysed hydrocyanation of norbornene. The lack of dissociation or interaction with HCN or alkenes has hindered mechanistic investigations, and is consistent with the requirement for elevated temperatures in order that the reaction can proceed with acceptable yields.

The mechanism necessarily requires the production of vacant coordination sites on palladium, either by dissociation of Pd(DIOP)$_2$ or by replacement of DIOP by HCN or alkene. The use of platinum and palladium complexes which are more reactive than Pd(DIOP)$_2$ has allowed the observation of species which may be important in the catalytic cycle, although it must be emphasised that in extrapolating such observations to suggest a mechanism, caution must be exercised, both for reasons mentioned earlier, and because the actual reaction proceeds at higher temperature and pressure than available in the N.M.R. studies.

The mechanism of ethene hydrocyanation catalysed by Ni[P(o-o-tolyl)$_3$]$_3$ has been deduced by McKinney and Roe from the DuPont laboratories. The fact that the productive catalytic cycle differs from that suggested two years earlier by Tolman from similar experiments, using the same complexes in the same laboratory, emphasises the difficulties encountered in mechanistic studies. The cycle of McKinney and Roe is described in Chapter One (section 1.4.4.).

The proposed mechanistic scheme for our system is shown below, (Scheme 17). The first step is the reaction of Pd(DIOP)$_2$

Scheme 17.   MECHANISTIC SCHEME.
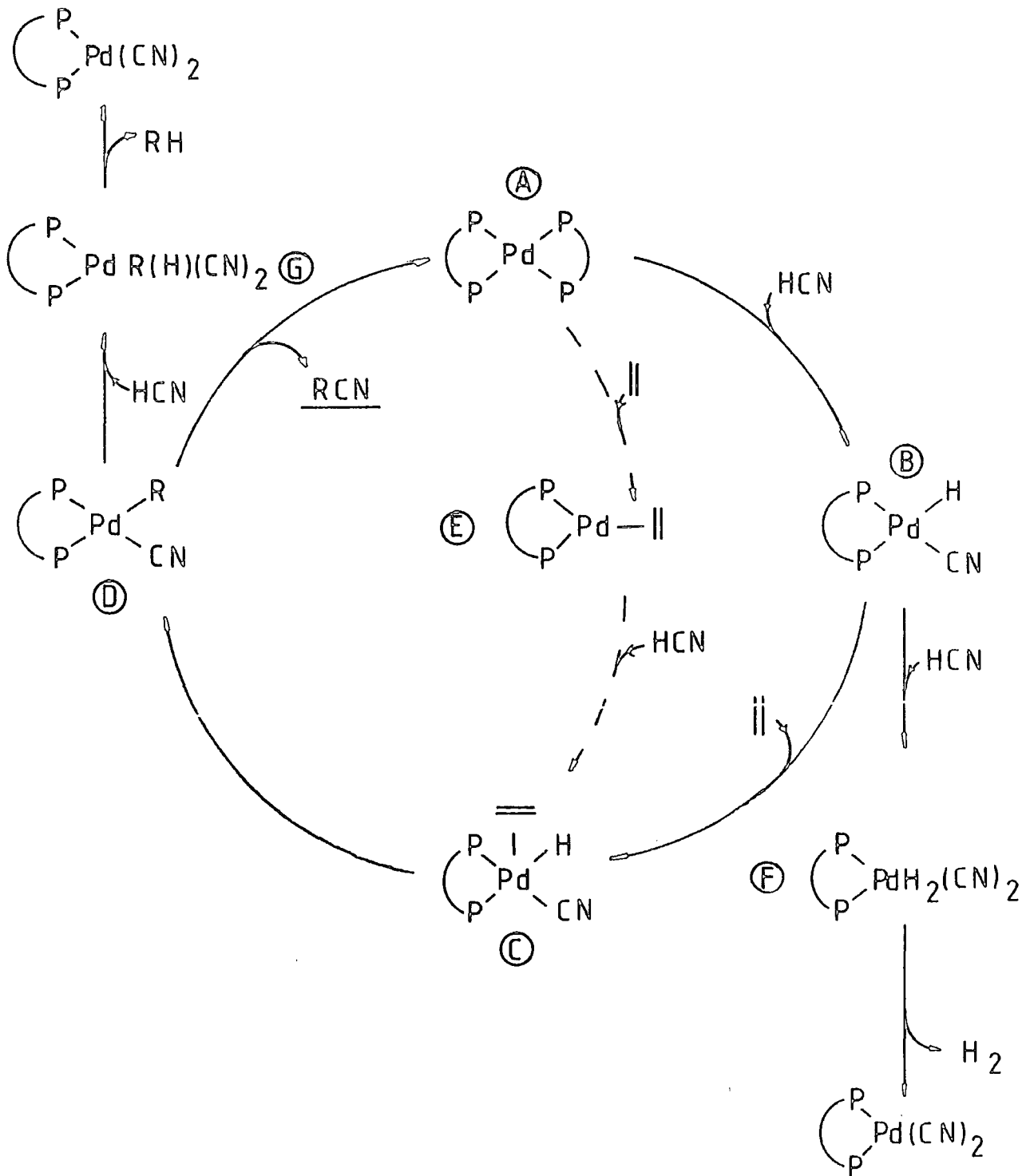
A. No information regarding the nature of this reaction was obtainable from this study. Dissociation of Pd(DIOP)$_2$ at high temperatures to give a 16 or 14 electron complex may occur. 14 electron complexes for monodentate phosphines have been observed and postulated as reactive intermediates, [45,46,55]. Direct reaction of HCN with A cannot be ruled out. Protonation of NiL$_4$ complexes increases ligand dissociation by 10^7 fold [6]. Pd(DIOP)$_2$ is stable to dissociation, and is inert to HCN and alkenes under conditions available for observation.

This study has shown that addition of HCN to a 16 electron DIOP palladium complex is rapid, generating the reasonably stable hydridocyanide B. This complex showed no reaction with a 200-fold excess of norbornene or norbornadiene; reaction of B with olefin may thus be rate limiting. Reaction of the olefin with B will give initially a five coordinate species C. An analogous platinum complex 18 was isolated by Baddley and

$$\begin{array}{ccc}
\text{Et}_3\text{P} & \overset{\overset{\text{H}}{|}}{\underset{|}{\text{Pt}}} & \text{C(CN)}_2 \\
\text{Et}_3\text{P} & \underset{\text{CN}}{} & \text{C(CN)}_2
\end{array}$$

18
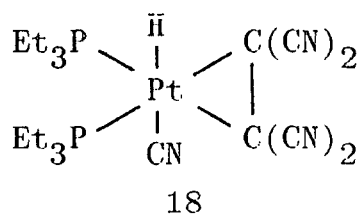
Uguagliati from the reaction of TCNE with PtHCN(PEt$_3$)$_2$, [56]. This intermediate species was not observed in these studies. β-cis hydride migration in C produces an alkyl metal cyanide, D, which is observable for the reaction containing ethene and (DIOP)Pd(H)CN.

The catalytic cycle is completed by a reductive elimination step. McKinney and Roe showed [7] that the reductive elimination step in the hydrocyanation of ethene catalysed by $Ni(0)[P(o-o-tolyl)_3]_3$ occurs via an associative process involving free ligand. If this were to occur in the $Pd(DIOP)_2$ case, the situation is complicated by the fact that DIOP is bidentate. Species containing monodentate DIOP have been postulated as intermediates in hydrocyanation reactions [4], and a related nickel complex 19 has been characterised by Tolman, [57].

19
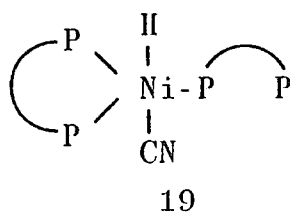
Although no evidence for the existence of such species has been found in these studies, their involvement cannot be excluded. The associative reduction elimination involving DIOP is shown in Scheme 18.

Another possibility for an associative reductive elimination is that shown in Scheme 19 involving coordination of olefin.

The reductive elimination step is, in common with other hydrocyanations, apparently irreversible, as no evidence for

$$\overset{P}{\underset{P}{\Bigl(}}Pd\overset{R}{\underset{CN}{\diagdown}} \quad + \quad P\frown P \quad \longrightarrow \quad \left[\overset{P}{\underset{P}{\Bigl(}}\underset{\underset{CN}{|}}{\overset{\overset{R}{|}}{Pd-P}}\frown P\right]$$

$$\overset{P}{\underset{P}{\Bigl(}}Pd\overset{P}{\underset{P}{\Bigr)}} \quad + \quad RCN$$

Scheme 18

$$\overset{P}{\underset{P}{\Bigl(}}Pd\overset{R}{\underset{CN}{\diagdown}} \quad + \quad \| \quad \longrightarrow \quad \left[\overset{P}{\underset{P}{\Bigl(}}Pd\overset{R}{\underset{CN}{\diagdown}}\right]$$

$$\overset{P}{\underset{P}{\Bigl(}}Pd-\| \quad + \quad RCN$$
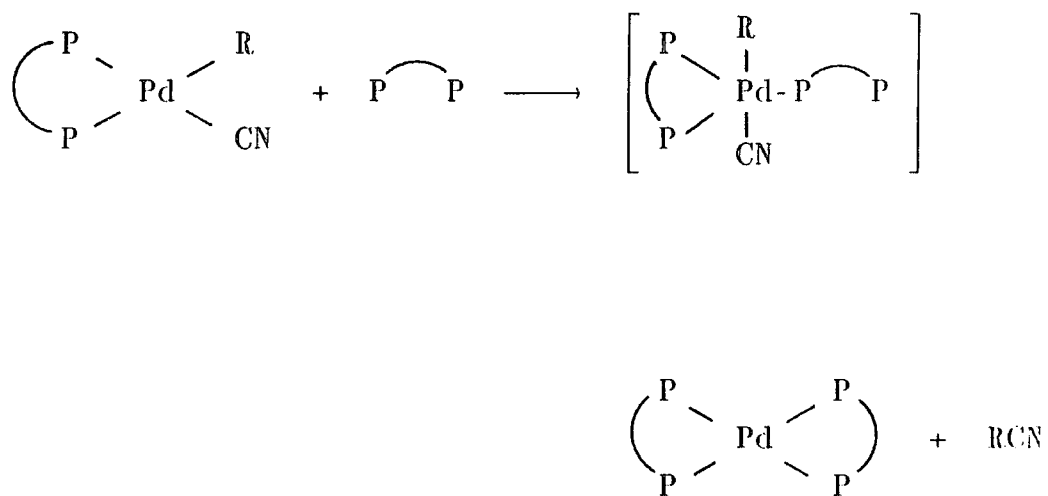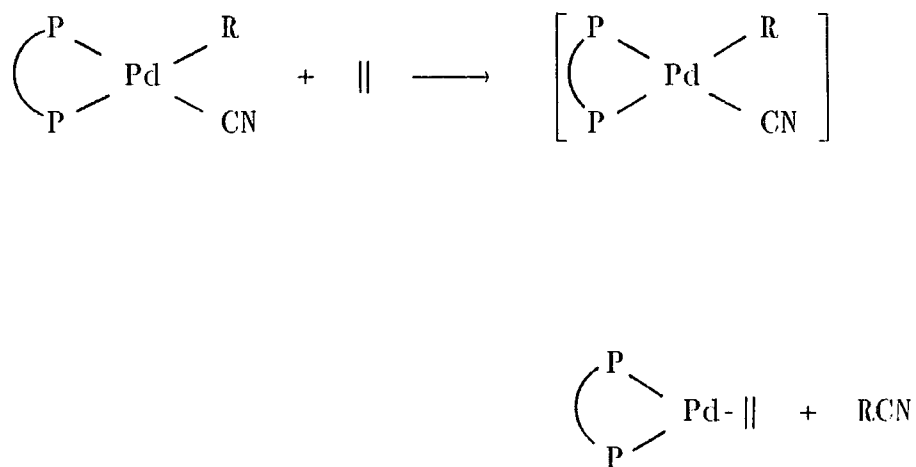
Scheme 19

interaction of various nitriles with $M(DIOP)_2$, $M(DIOP)Alkene$ or $M(DIOP)H(CN)$ (M = Pd, Pt) has been found.

The 'unsaturate' route, in which olefin binding to give E: precedes oxidative addition to HCN is also shown in Scheme 17. This pathway is considered less likely due to the stability of

the hydridocyanide generated from the olefin complexes in the presence of a large excess of olefin.

To complete the mechanistic scheme, the removal of palladium from the catalytic cycle by reaction of B and/or D with excess HCN is indicated. These reactions may occur via Pd(IV) intermediates, F and G which on reductive elimination of alkane or hydrogen respectively, give $(DIOP)Pd(CN)_2$ which is catalytically inactive, and may decompose to give $Pd(CN)_2$. Hexacoordinate palladium(IV) species have been proposed as intermediates in the reactions of alkyl halides with bis(phosphine)dialkyl palladium(II) complexes, [58].

3.6. STUDIES OF SYSTEMS WITH OTHER PHOSPHORUS LIGANDS

Mechanistic studies of other systems were much less successful than those of DIOP.

3.6.1. BPPM System

$Pd(BPPM)_2$ catalyses the asymmetric hydrocyanation of norbornene to give similar preparative yields, and greater optical yields than those obtained with $Pd(DIOP)_2$. [31]P N.M.R. studies of the interaction of BPPM complexes were therefore undertaken. BPPM differs from DIOP in that the two phosphorus atoms are not related by a C_2 symmetry element. They have ^{31}P chemical shifts of -8 for the secondary phosphine and -20 ppm for the primary phosphine [59]. Even in complexes with each phosphine trans to an identical ligand, P-P coupling can occur, which should provide additional parameters to characterise the system. Unfortunately the spectra are complicated by the possibility of hindered rotation about the amide bond producing rotamers, [60]. The variation of the [31]P N.M.R. spectrum of

BPPM is shown in <u>Figure 15</u>. There is also the possibility of fluxional behaviour in the chelate ring akin to that observed for Pd(DIOP)$_2$, [10]. The dynamic behaviour of chelate rings can render very complex spectra, e.g. in the ^{31}P N.M.R. spectrum of Rh$^+$(DIOP)$_2$ simplified by cooling, there are three phosphorus resonances, each phosphorus is coupled differently to rhodium. and they are coupled differently to each other [61].

(BPPM)PdCl$_2$ was prepared in an analogous manner to (DIOP)PdCl$_2$. The ^{31}P N.M.R. data for this simple complex.

δ_{Pa1} 43.1

δ_{Pa2} 42.8   all doublets with $^2J_{P,P}$ = 10 Hz

δ_{Pb1} 25.4   (in CH$_2$Cl$_2$ 298 K)

δ_{Pb2} 23.7

The presence of 2 signals for each phosphorus is most likely caused by the existence of rotomers. Reduction of (BPPM)PdCl$_2$ with sodium borohydride in the presence of excess BPPM gave the yellow palladium(0) complex Pd(BPPM)$_2$. The ^{31}P N.M.R. spectrum of the complex contained two triplets δ_{Pa}36.0 ppm, δ_{Pb} -3.3 ppm J_{PaPb} 20 Hz, caused by an A$_2$B$_2$ system. The presence of free BPPM gave additional sharp resonances at the positions of free BPPM, indicating that no exchange with free ligand occurred at room temperature. For comparison, addition of 2 equivalents of BPPM to a toluene solution of Pd(dba)$_2$ discharged the intense violet colour of the Pd(dba)$_2$ leaving an orange solution with broad ^{31}P resonances at δ 36.0 and δ -3.3 ppm as well as several other broad, unexplained resonances.

Addition of HCN to solutions of Pd(BPPM)$_2$ did not alter the ^{31}P spectra. Peaks at δ 30.4 and δ 32.5 were identified as BPPM

Figure 15. VARIATION OF PHOSPHORUS N.M.R. SPECTRUM OF BPPM WITH TEMPERATURE.
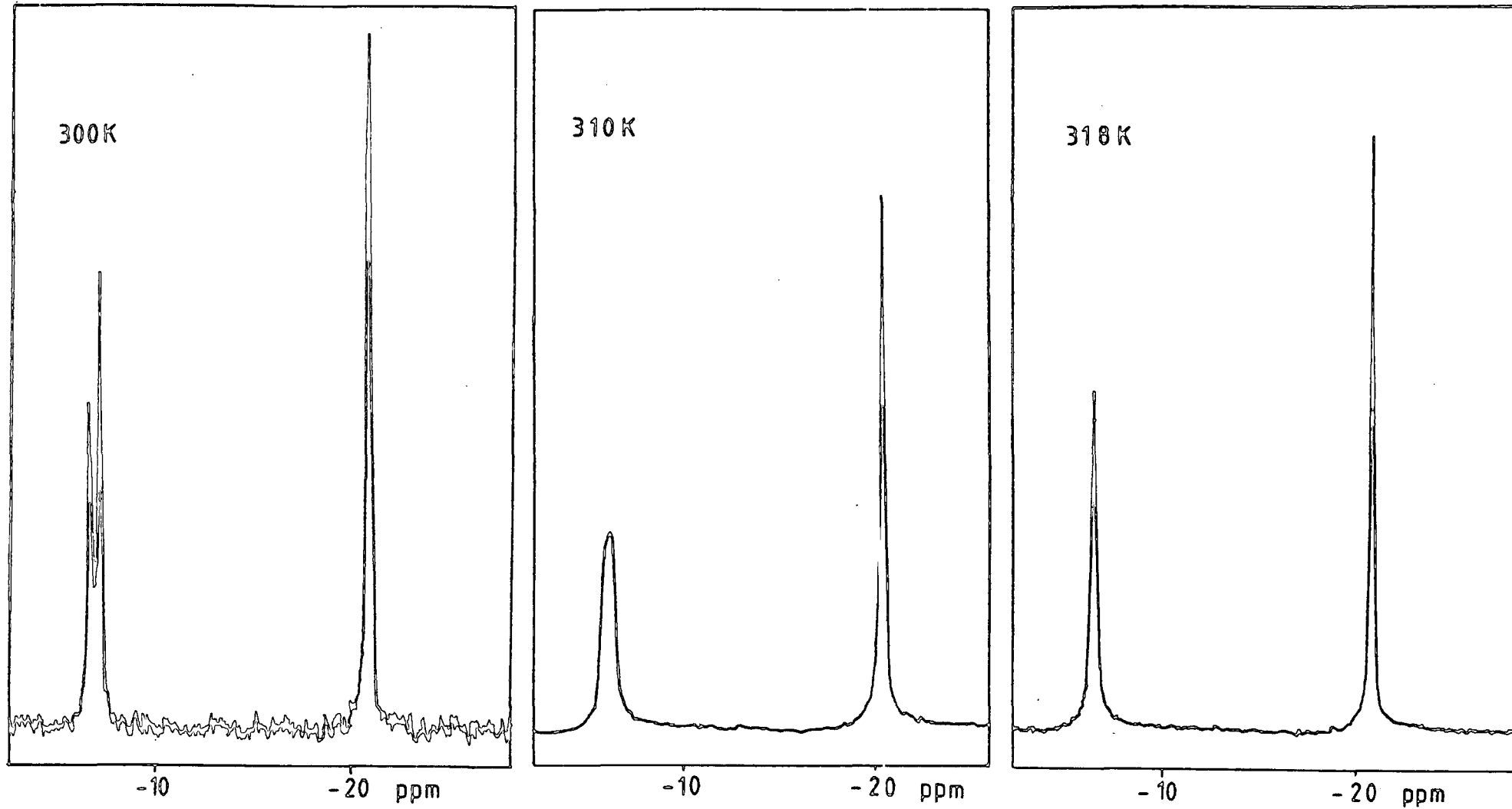
oxide (present in small amounts in some spectra), by the addition of an oxidised sample of BPPM to the solutions.

(BPPM)PtCl$_2$ was prepared from (^{t}BuCN)$_2$PtCl$_2$. The ^{31}P N.M.R. spectral parameters were,

δ_{Pa1} 25.9 ppm

δ_{Pa2} 25.4   all doublets with $^2J_{P,P}$ 18 Hz

δ_{Pb1} 2.0

δ_{Pb2} 0.4

$^1J_{Pa1Pt} = {}^1J_{Pa2Pt} = 3556$ Hz

$^1J_{Pb1Pt} = 3475$ Hz $^1J_{Pb2Pt} = 3488$ Hz

(in CDCl$_3$, 298 K)

Reduction of BPPM PtCl$_2$ with sodium borohydride in ethanol/methylene chloride in the presence of ethene gave a white amorphous solid which dissolved in toluene to give a homogeneous solution, the ^{31}P N.M.R. of which contained two platinum coupled resonances each resonance was split into at least four further lines involving P,P coupling and rotational isomers.

δ_{Pa} 50.0 ppm $^1J_{PaPt}$ 3800 Hz

δ_{Pb} 10.0 ppm $^1J_{PtPt}$ 3440 Pt

These resonances were ascribed to (BPPM)Pt ethene. Addition of 10 equivalents of norbornene generated (BPPM)Pt norbornene with

δ_{Pa} 51.0 ppm $^1J_{PaPt}$ 3682 Hz

δ_{Pb} 9.3 ppm $^1J_{PbPt}$ 3255 Hz

The complex was also isolated by carrying out the reaction in THF and removing the solvent in vacuo.

HCN was added to solutions of (BPPM)Pt ethene and (BPPM)Pt norbornene. The initial resonances of alkene complexes

vanished, leaving broad complicated spectra containing many peaks between $\delta^{31}P$ 30.5 ppm and -8.5 ppm. None of the reaction solutions appeared to have hydride resonances in their ^1H N.M.R. spectra.

In conclusion, the BPPM complexes appear to react similarly to those of DIOP, however analysis of the reactions is made difficult by complicated N.M.R. spectra. The ^{31}P N.M.R. spectrum of (BPPM)PtCl$_2$ is shown in Figure 16.

3.6.2. The BINAP System

Use of the complex Pd(BINAP)$_2$ in the hydrocyanation of norbornene gave low chemical, but the highest optical yields.

Addition of BINAP to a toluene or CH$_2$Cl$_2$ solution of Pd(dba)$_2$ showed by ^{31}P N.M.R. that the equilibrium in Scheme 20

$$2BINAP \ + \ Pd(dba)_2 \ \rightleftharpoons \ Pd(BINAP)_2 \ + \ 2dba$$
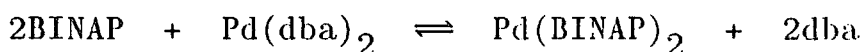
Scheme 20

lies to the left. The steric bulk of the ligand is likely to be the cause for the reluctance to coordinate, and may explain the low catalytic activity of the Pd/BINAP system.

3.6.3. The Triphenylphosphite System

The zerovalent palladium complex of triphenylphosphite is an efficient catalyst for the addition of HCN to a range of alkenes, including norbornene [31,62]. The complex was first prepared by heating four equivalents of triphenylphosphite with palladium(0) bis-p-tolyl-isonitrile in benzene, [63]. The complex was purified by recrystallization from ethanol. The formulation of the complex as PdL$_4$ was based on phosphorus and

Figure 16. PHOSPHORUS N.M.R. SPECTRUM OF BPPM Pt Cl$_2$.
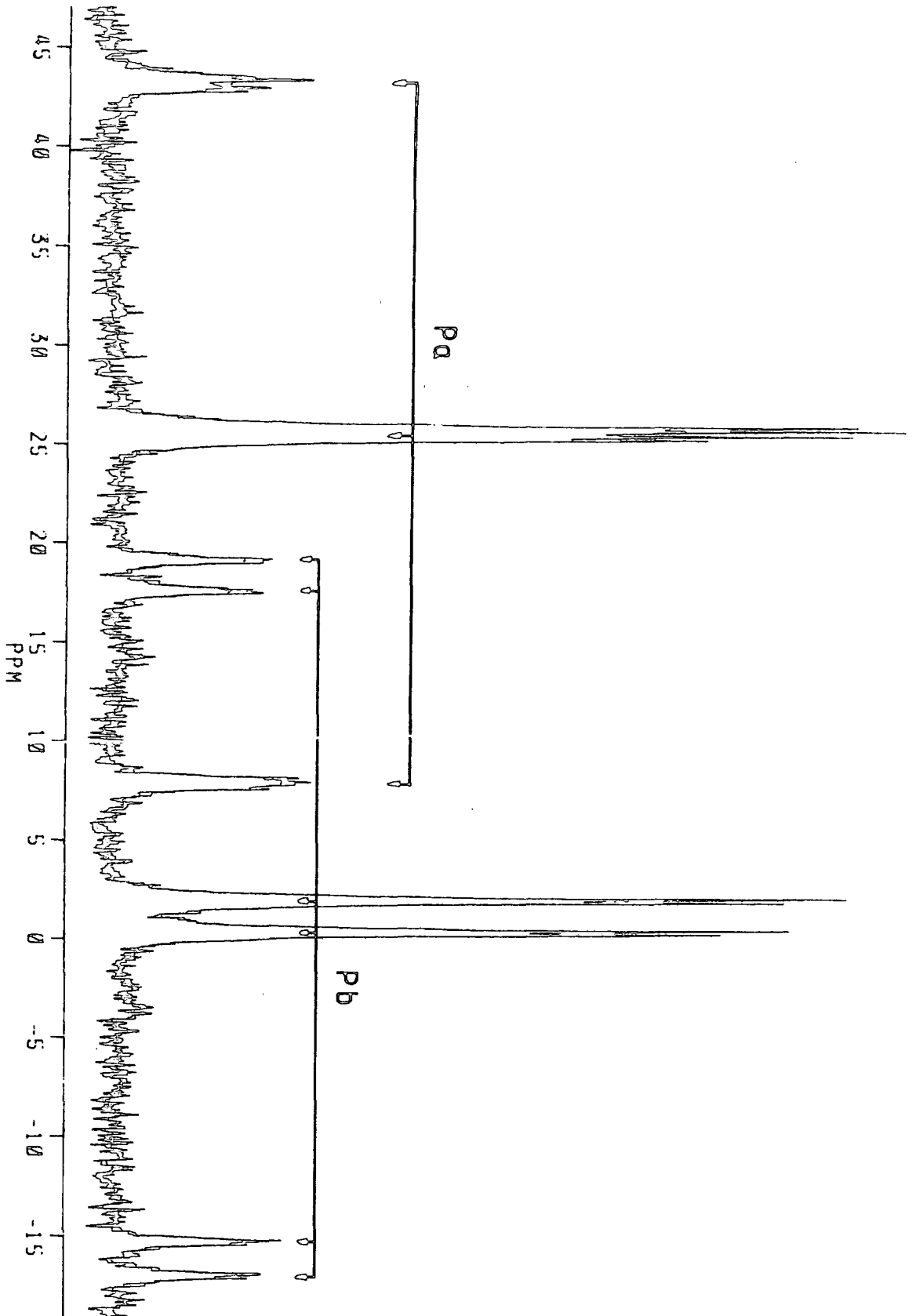
palladium elemental analysis. The cryoscopic molecular weight of the complex in benzene was found to be 380 ($C_{72}H_{60}O_{12}P_4Pd$, M = 1347). This implies extensive dissociation in solution, however Tolman has shown that some palladium(0) and nickel(0) complexes which have a low reported cryoscopic molecular weight do _not_ dissociate in solution, and he points out that cryoscopic molecular weight determinations ought to be treated with caution in the absence of confirmatory evidence, [16]. More recently, a related preparation has been described, involving displacement of PPh_3 from zerovalent $Pd(PPh_3)_4$ using excess triphenylphosphite, [64]. The complex may also be prepared by reducing a suspension of bistriphenylphosphite palladium dichloride in ethanol with hydrazine hydrate, [63]. This was the method chosen to prepare the complex used in this study.

The ^{31}P N.M.R. spectrum of the complex consisted of a single sharp resonance at $\delta^{31}P$ 137.0. No spectral change was observed in the temperature range 205 to 316 K in $CHCl_3$. An upper limit of $K_d = 8 \times 10^{-6}$ M can be estimated as no free ligand was detected in the spectrum. On addition of 17 mg of $P(OPh)_3$ to 66 mg of the complex, a resonance appeared at $\delta^{31}P$ 127.0 ppm. However both the free ligand and bound signals were broad. Raising the temperature caused the peaks to broaden further. The addition of another 19 mg of free ligand broadened the peaks further still, and raising the temperature led eventually to coalescence. This behaviour is _not_ consistent with a dissociative exchange of ligand from $Pd[P(OPh)_3]_4$, Scheme 21. The same behaviour was found for the system in toluene and chloroform, and for a sample of complex purified by

recrystallization from ethanol.

$$PdL_4 \rightleftharpoons PdL_3 + L$$
$$PdL_3 + L^* \rightleftharpoons PdL_3L^* \qquad L, L^* = P(OPh)_3$$

Scheme 21
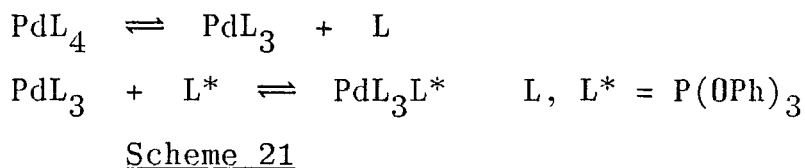
If dissociative exchange were occurring, then the linewidth of the bound ligand resonances would be independent of added ligand, as the lifetime of the ligand in the complex would be determined solely by the rate of dissociation of the ligand from the tetrakis complex.

The involvement of a 20 electron PdL_5 complex (Scheme 22) is highly improbable.

$$PdL_4 + L^* \rightleftharpoons PdL_4L^* \rightleftharpoons PdL_3L^* + L$$

Scheme 22
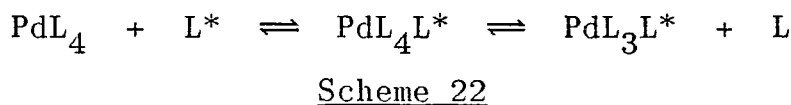
If the palladium complex were tris-triphenylphosphite palladium(U) rather than tetrakis-triphenylphosphite palladium(0), then the exchange could readily be explained in terms of an associative exchange via the 18 electron four coordinate intermediate in Scheme 23.

$$PdL_3 + L^* \rightleftharpoons PdL_3L^* \rightleftharpoons PdL_2L^* + L$$

Scheme 23
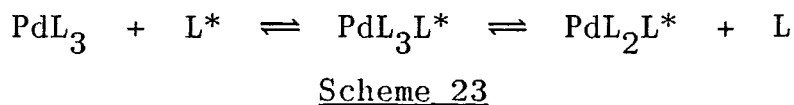
If it is assumed that the lifetime of the ligand in the PdL_4 intermediate is small, then the ratio of the lifetime of the ligand in the complex, τ_c, to the lifetime of the free

ligand, τ_f, should be related to the ratio of the concentrations of complex and free ligand by,

$$\frac{\tau_c}{\tau_f} = \frac{3[PdL_3]}{[L]}$$

The linewidths of the resonances due to free and bound ligand for the two concentrations of added free ligand are shown in Table 6 and Table 7. The lifetimes τ_c and τ_f calculated from these linewidths are also shown, together with the ratio τ_c/τ_f.

TABLE 6. Variation of Linewidths with Temperature, for [L] = 2.74 x 10^{-2} M [PdL$_3$] = 3.18 x 10^{-2} M[a]

T(K)	δ 137 (Complexed ligand)		δ 127 (Free ligand)		Ratio $\frac{\tau_c}{\tau_f}$
	$\omega_{\frac{1}{2}}$ (Hz)	τ_c (S)	$\omega_{\frac{1}{2}}$ (Hz)	τ_f (S)	
260	70	4.9 x 10^{-3}	75	4.5 x 10^{-3}	1.1
270	80	4.24 x 10^{-3}	200	1.63 x 10^{-3}	2.6
282	100	3.35 x 10^{-3}	300	1.08 x 10^{-3}	3.1

[a] These concentrations give $\dfrac{3[PdL_3]}{[L]}$ = 3.48.

The spectra from which the data in Table 7 were taken are shown in Figure 17. The lifetimes of free and complexed ligand fit the suggested relationship to the concentrations better in Table 7 than in Table 6. The drop in the τ_c/τ_f ratio with temperature may be caused by the complex beginning to

Figure 17. PHOSPHORUS N.M.R. SPECTRA RELATED TO TABLE 7.

290 K

300 K

301 K

311 K
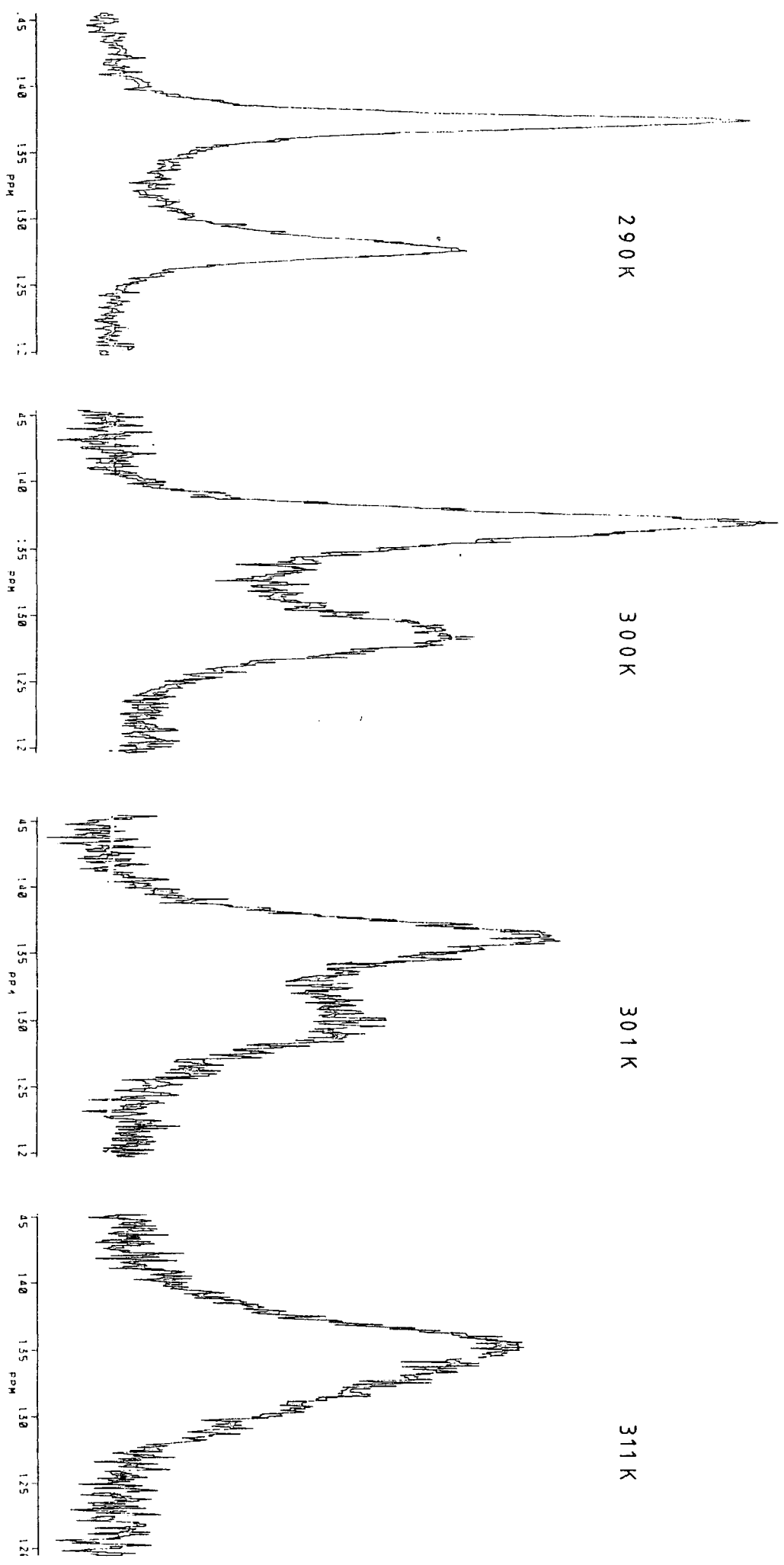
TABLE 7. Variation of Linewidths with Temperature, for
$[L] = 5.80 \times 10^{-2}$ M $[PdL_3] = 3.18 \times 10^{-2}$ M[a]

T(K)	δ 137 (Complexed ligand)		δ 127 (Free ligand)		Ratio $\dfrac{\tau_c}{\tau_f}$
	$\omega_{\frac{1}{2}}$ (Hz)	τ_c (S)	$\omega_{\frac{1}{2}}$ (Hz)	τ_f (S)	
270	121	2.74×10^{-3}	150	2.6×10^{-3}	1.1
280	135	2.45×10^{-3}	211	1.5×10^{-3}	1.6
290	250	1.30×10^{-3}	390	8.2×10^{-4}	1.6
301	395	8.20×10^{-4}	640	5.0×10^{-4}	1.6

[a] These concentrations give $\dfrac{3[PdL_3]}{[L]} = 1.6$.

precipitate from solution at lower temperatures. This theory is supported by a drop in the integral of the complexed ligand resonance at low temperatures.

The above data supports the formulation of the complex as PdL_3. However this explanation requires that the product from the reduction of $Pd[P(OPh)_3]_2Cl_2$ in the presence of 2.2 equivalents of $P(OPh)_3$ is pure $Pd(P(OPh)_3)_3$. The preparation of $Pd(P(OPh)_3)_3$ is mentioned briefly in the literature. It is formed by reacting (π-methallyl $PdCl)_2$ in benzylamine with triphenylphosphite. Little characterization of the complex is given and it is described as "otherwise not easily accessible", [65].

It is often difficult to obtain reliable analyses for metal complexes, and the difference between expected values for PdL_3 and PdL_4 is relatively small. Throughout the early literature,

the designation of the zerovalent palladium triphenylphosphite complex as PdL_4 rather than PdL_3 appears to be based solely on elemental analysis. The theoretical analytical figures, and values obtained in this and other studies are summarised in Table 8.

TABLE 8. Analytical Data for PdL_4 vs. PdL_3

	Theoretical (%)			Found (%)	
	PdL_4	PdL_3	This Study	Ref. 64 (for PdL_4)	Ref. 66 (for PdL_3)
Pd	7.9	10.27	9.89	7.85	11.26
P	9.21	8.97	8.72	9.4	8.34

The analysis for the complex made in this study agrees well with the formulation PdL_3.

Mass spectral analysis of the complex provided no useful information, the spectra consisted only of ligand fragments.

In order to investigate the system slightly further a solution of palladium(0) bis-dibenzylideneacetone was titrated with triphenylphosphite. Triphenylphosphite was added to give palladium to phospite ratios of 1:2, 1:3, 1:4 and 1:5.5. The spectra contained resonances from three species. Complexed ligand at δ 137, a system with δ_{Pa} 135.6 ppm, δ_{Pb} 130.9 ppm J_{PaPb} = 21 Hz, and free ligand at δ 126. When the ratio was 1:2 the spectrum contained a sharp bound ligand resonance at δ 137 together with a major signal δ_{Pa} 135.6, δ_{Pb} 130.9 (Figure 18).

Figure 18. PHOSPHORUS N.M.R. SPECTRA RELATED TO PHOSPHITE ADDITION.
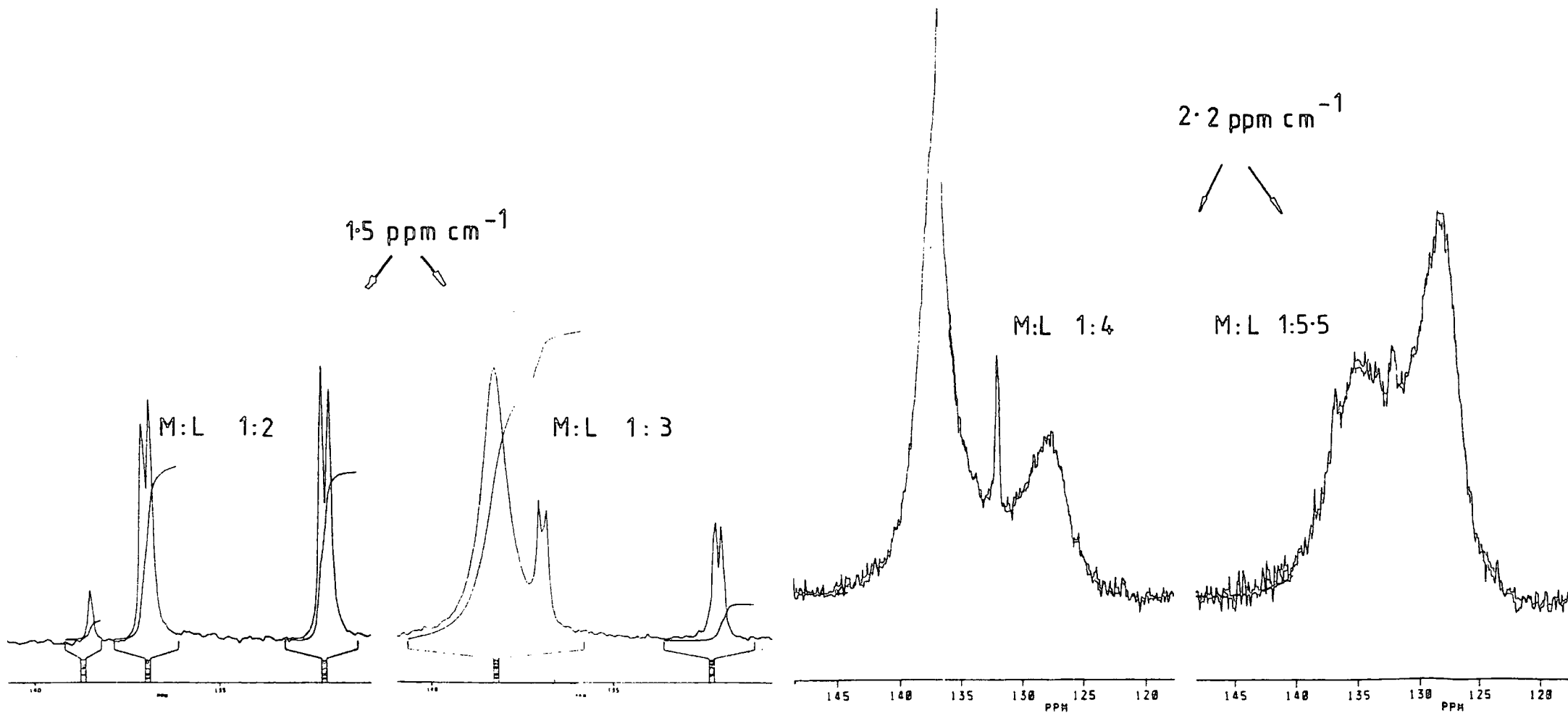
This may be due to a complex containing bridging dba ligands. Similar Pd complexes have been observed [66]. This spectrum remained unchanged for five days at room temperature. Raising the ratio to 1:3 left a trace of the P,P coupled resonance, but the spectrum consisting mostly of the bound ligand resonance at δ 137. No free ligand was present in the spectrum. On addition of four equivalents of phosphite, the spectrum contained an exchange broadened system with complexed ligand at δ 137 $\omega_{\frac{1}{2}}$ 200 Hz, free ligand at δ 127 $\omega_{\frac{1}{2}}$ 585 Hz which gives τ_c/τ_f = 3.0 and $3[PdL_3]/[L]$ = 3.0. The integrated areas of the complexed and bound ligand resonances were in the ratio 3:1. The peaks began to coalesce at 297 K. When the amount of ligand was increased to 5.5 equivalents, the peaks were so broad they began to overlap.

The N.M.R. data appears to be consistent with the formulation of the complex as PdL_3.

The interaction of the complex with other components of the hydrocyanation reaction was examined. No change in the [31]P N.M.R. spectrum was observed when the olefins norbornene or vinyl acetate were added to the complex either in the presence or absence of added free triphenylphosphite. Surprisingly, no change in the [31]P N.M.R. was observed when 14 equivalents of HCN were added to a solution of the complex in methylene chloride, even after several hours at 278 K. If the complex is the 16 electron PdL_3 complex, it would be expected to be quite reactive to addition.

REFERENCES

1. (a) B.R. James, "Comprehensive Organometallic Chemistry", G. Wilkinson, F.G.A. Stone, E.W. Abel, Eds., Pergamon Press, New York 1982, Vol. 8, Ch. 51 p. 353.

    (b) E.S. Brown, Aspects Homogeneous Catal., 57, (1974).

2. J.P. Collman and L.S. Hegedus, "Principles and Applications of Organotransition Metal Chemistry", University Science Books, (1980).

3. J.E. Backvall and O.S. Andell, J. Chem. Soc. Chem. Commun., 1098, (1981).

4. W.R. Jackson and C.G. Lovel, Aust. J. Chem., 35, 2053-67, (1982).

5. C.A. Tolman, W.C. Seidel, J.D. Druliner and P.J. Domaille, Organometallics, 3, 33-38, (1984).

6. C.A. Tolman, R.J. McKinney, W.C. Seidel, J.D. Druliner and W.R. Stevens, Adv. Catal., 33, 1-46, (1985).

7. R.J. McKinney and D.C. Roe, J. Amer. Chem. Soc., 108, 5167-5173, (1986).

8. J. Halpern and C.S. Wong, J. Chem. Soc. Chem. Commun., 629, (1973).

9. (a) J. Halpern, Trans. Am. Crystallogr. Assoc., 14, 59, (1978).

    (b) J. Halpern, T. Okamoto and A. Zakhariev, J. Mol. Cat., 2, 65, (1976).

    (c) J. Halpern, in "Organotransition Metal Chemistry", Y. Ishida and M. Tsutui, eds. Plenum, 1975 p. 109.

10. K. Brown and P.A. Challoner, J. Organomet. Chem., 217, C25-28, (1981).

11. P.S. Elmes and W.R. Jackson, J. Amer. Chem. Soc., 101, 6128, (1979).

12. R.K. Harris, "Nuclear Magnetic Resonance Spectroscopy, A Physicochemical View", Pitman, London, (1983).

13. F.P. Gasparro and N.H. Kolodny, J. Chem. Ed., 54, 259, (1977).

14. G. Binsch, J. Amer. Chem. Soc., 91, 1304, (1969).

15. C.A. Tolman, J. Amer. Chem. Soc., 96, 2780, (1974).

16. C.A. Tolman, W.C. Seidel and D.H. Gerlach, J. Amer. Chem. Soc., 94, 2669 (1972).

17. C.A. Tolman and W.C. Seidel, J. Amer. Chem. Soc., 96, 2774, (1974).

18. C.A. Tolman, Inorg. Chem., 10, 1540, (1971).

19. J.M. Brown, S.J. Cook and S.J. Kimber, J. Organomet. Chem., 269, C58-60, (1984).

20. J.P. Collman and L.S. Hegedus, "Principles and Applications of Organometallic Chemistry", University Science Books, Mill Valley, California, (1980).

21. A. Panuzi, A. De Renzi, R. Palumbo and G. Pasaro, J. Amer. Chem. Soc., 91, 3879, (1960).

22. J.F. Nixon and A. Pidcock, Ann. Rev. N.M.R. Spec., 2. 346, (1969).

23. A. Pidcock, R.E. Richards and L.M. Venanzi, J. Chem. Soc. (A), 1707, (1966).

24. F.H. Allen and A. Pidcock, J. Chem. Soc. (A), 2700, (1968).

25. C.H. Langford and H.B. Gray, "Ligand Substitution Processes", Benjamin, New York, (1965).

26. T.G. Appleton, M.A. Bennett and I.B. Tomkins, _J. Chem. Soc. Dalton_, 439, (1976).

27. G.C. Mather, G.J.N. Rapsey and A. Pidcock, _Inorg. Nucl. Chem. Lett._, 9, 567, (1973).

28. J. Chatt and B.L. Shaw, _J. Chem. Soc._, 5075, (1962).

29. J. Tsuji and H. Hakatashi, _J. Amer. Chem. Soc._, 87, 3275, (1965).

30. E.S. Brown, in "Organic Synthesis by Metal Carbonyls", eds. I. Wender and P. Pino, Wiley, New York, 1965, VII p. 655.

31. P.S. Elmes and W.R. Jackson, _Aust. J. Chem._, 35, 2041-51, (1982).

32. R.S. Paonessa, A.L. Prignaro and W.C. Trogler, _Organometallics_, 4, 647-657, (1985).

33. F.R. Hartley, "The Chemistry of Platinum and Palladium", Applied Science Publishers Ltd., London, 1973 p. 441.

34. L. Malatesta and S. Cenini, "Zerovalent Compounds of Metals", Academic Press, New York, 1974.

35. R. Van der Linde and R.O. DeJohgh, _J. Chem. Soc. Chem. Commun._, 563, (1971).

36. A. Visser, R. Van der Linde and R.O. DeJohgh, _Inorg. Synth._, 16, 127, (1976).

37. J.M. Brown, Private communication.

38. P.T. Cheng, C.D. Cook, C.H. Koo, S.C. Nyburg and M.T. Shiomi, _Acta Crystallogr. sect. B_, 27, 1904, (1971).

39. P.T. Cheng, C.D. Cook, S.C. Nyburg and K.Y. Wan, _Inorg. Chem._, 10, 2210, (1971).

40. K.F. Purcell and J.C. Kotz, "Inorganic Chemistry", Holt Saunders, Toronto, (1977).

41. C. Moore, <u>Nat. Bur. Stand. (USA)</u>, No. 467, <u>2</u>, (1952), <u>3</u>, (1953).

42. V. Gramlich and G. Consiglio, <u>Helv. Chim. Acta</u>, <u>62</u>, 1016, (1979).

43. C. Panattoni, G. Bomliveri, U. Belluco and W.H. Baddley, <u>J. Amer. Chem. Soc.</u>, <u>90</u>, 798, (1968).

44. J. Halpern and T.A. Weit, <u>J. Chem. Soc. Chem. Commun.</u>, 631, (1973).

45. E. Negishi, <u>Acc. Chem. Res.</u>, <u>15</u>, 340, (1982).

46. S.D. Ittel and J.A. Ibers, <u>Adv. Organomet. Chem.</u>, <u>14</u>, 33-62, (1974).

47. (a) B.M. Trost, T.R. Verhoeven, <u>J. Amer. Chem. Soc.</u>, <u>102</u>, 4730, (1980).

    (b) P.R. Auburn, P.B. Mackenzie and B. Bosnich, <u>J. Amer. Chem. Soc.</u>, <u>107</u>, 2033, (1985).

48. A.V. Kramer and J.A. Osborn, <u>J. Amer. Chem. Soc.</u>, <u>96</u>, 7832, (1974).

49. T.T. Tsou and J.K. Kochi, <u>J. Amer. Chem. Soc.</u>, <u>101</u>, 6319, (1979).

50. G.A. Lane, W.E. Geiger and N.G. Conholy, <u>J. Amer. Chem. Soc.</u>, <u>109</u>, 402, (1987).

51. J.A. Labinger, J.A. Osborn and N.J. Coville, <u>Inorg. Chem.</u>, <u>19</u>, 3236-43, (1980).

52. J.K. Stille and S.Y.K. Lau, <u>Acc. Chem. Res.</u>, <u>10</u>, 434-442, (1977).

53. (a) J.K. Kochi, <u>Acc. Chem. Res.</u>, <u>7</u>, 351 (1974).

    (b) M.L. Poutsma, <u>Free Radicals</u>, <u>2</u>, 169, (1973).

54. P. Filton and E.A. Rick, J. Organometal. Chem., 28, 287, (1971).

55. E. Negishi, T. Takahashi and K. Akiyoshi, J. Chem. Soc. Chem. Commun., 1338, (1986).

56. W.H. Baddley and P. Uguagliati, J. Amer. Chem. Soc., 90, 5446, (1958).

57. J.D. Druliner, A.D. English, J.P. Jesson, P. Meakin and C.A. Tolman, J. Amer. Chem. Soc., 98, 2156, (1976).

58. (a) A. Gille and J.K. Stille, J. Amer. Chem. Soc., 102, 4933-4941, (1980).

(b) D. Molstein and J.K. Stille, J. Amer. Chem. Soc., 101, 4981, (1979).

(c) D. Milstein and J.K. Stille, J. Amer. Chem. Soc., 101, 4992, (1979).

(d) D. Milstein and J.K. Stille, J. Amer. Chem. Soc., 103, 4174, (1982).

59. J.K. Stille and G. Pierson, J. Mol. Catal., 21, 203-10, (1983).

60. I. Ojima, T. Kogure and N. Yoda, J. Org. Chem., 45, 4728. (1980).

61. P.A. Chaloner, J. Organometal. Chem., 266, 191-201, (1984).

62. E.S. Brown and E.A. Rick, J. Chem. Soc. Chem. Commun., 112, (1969).

63. L. Malatesta and M. Angoletta, J. Chem. Soc., 1186-88, (1957).

64. S. Yamazaki, Inorg. Chem., 21, 1638-40, (1982).

65. W. Kuran and A. Musco, J. Organometal. Chem., 40, C47-48. (1972).

66. E. Uhlig, E. Dinjus and R. Schlegel, Z. Chem., 16, 408-9. (1976); Chem. Abstr., 86, 37101K.

CHAPTER 4

CATALYTIC AND STOICHIOMETRIC TRANSFORMATIONS WITH

TRIPHENYL(P,P,P-TRIPHENYLPHOSPHINE IMIDATO-N)

PHOSPHORUS CYANIDE, PNP$^+$CN$^-$

4.1. INTRODUCTION

The need for non-hygroscopic organic soluble cyanide salts was outlined in the Introduction (section 1.5.). The preparation of anhydrous triphenyl(P,P,P-triphenylphosphine imidato-N)phosphorus cyanide 1a and chloride 1b (hereafter called PNP$^+$CN$^-$ and PNP$^+$Cl$^-$) was described in 1977 by Martinsen

$$\text{Ph}_3\text{P=}\overset{+}{\text{N}}\text{=PPh}_3\text{X}^- \qquad \text{1a} \quad \text{X}^- = \text{CN}^-$$
$$\text{1b} \quad \text{X}^- = \text{Cl}^-$$

and Songstad, [1]. The synthetic utility of these salts as phase transfer catalysts and for stoichiometric displacements, particularly for hydrolysis-sensitive substrates, was examined in this study.

4.2. PREPARATION AND STABILITY OF PNP SALTS

PNP salts are expensive at present, as there is no large scale use for them, although the starting materials for the preparation are relatively inexpensive. The method of preparation used in this study was based on that described by Ruff and Schloetz. Triphenylphosphine was reacted with chlorine in dry 1,1,2,2-tetrachloroethane at -25°C. The solution of Ph$_3$PCl$_2$ thus formed was refluxed with triphenylphosphine and hydroxylamine hydrochloride for 8 hours to give PNP chloride, triphenylphosphine oxide and HCl. The preparation, summarised in Scheme 1 was conducted on a large scale (~ 200 g product) in order to minimise losses due to inaccurate measurement of the

chlorine added.

$$2Ph_3P \ + \ 2Cl_2 \ \xrightarrow[\quad N_2 \quad]{-25^{\circ}C, \ C_2H_2Cl_4} \ 2Ph_3PCl_2$$

$$2Ph_3PCl_2 \ + \ Ph_3P \ + \ NH_2OH.HCl \ \longrightarrow \ PNP^+Cl^- \ + \ Ph_3P{=}O \ + \ HCl\uparrow$$
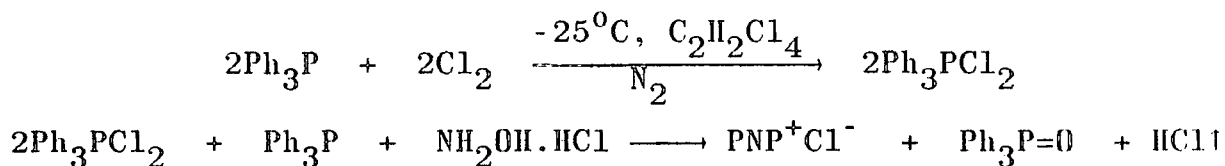
Scheme 1

The conversion of PNP^+Cl^- to PNP^+CN^- was achieved by one of two methods, based on those in the literature, [1]. The first method was to treat a dilute solution of PNP^+Cl^- with a 30-fold excess of dilute potassium cyanide solution to precipitate PNP^+CN^- from solution, which was then recrystallised. The dilute solutions are necessary to minimise co-precipitation of the hydroxide. The second involved adding one equivalent of KCN to a warm concentrated methanol solution of PNP^+Cl^-, under N_2. A further equivalent of KCN was added to the solution after removal of precipitated KCl to ensure complete conversion. The PNP^+CN^- was further purified by recrystallisation after removal of the methanol, in vacuo.

The latter method was preferentially used, despite the more complicated manipulations involved, as the PNP^+CN^- was obtained in greater yield and higher purity from this technique. PNP^+CN^- could be obtained as fine white crystals by recrystallization from acetone/ether provided that the crude PNP^+CN^- was dissolved in the minimum volume of dry O_2-free acetone. Oxygen free ether was then added until the slightest turbidity was detected in the solution, which was then cooled to $5^{\circ}C$ and left for 72 to 96

hours for the crystals to form. The crystals were separated by
filtration under N_2, and dried in vacuo before use. Many PNP
salts are slow to crystallise, [3].

PNP^+CN^- and PNP^+Cl^- are non-hygroscopic; samples of the
salts remained free flowing and crystalline after many weeks
exposure to atmospheric moisture in open topped containers;
however due to the fine nature of the crystals the salts were
heated to $70^\circ C$ for 3 hours at 0.01 mmHg to remove any trapped
surface moisture. Solid PNP^+CN^- and PNP^+Cl^- are both air
stable, although solutions of PNP^+CN^- in acetone or CH_3CN
rapidly turn brown on exposure to air. Songstad suggests from
I.R. spectra that this decomposition is due to the formation of
PNP^+OCN^- [1,3], hence the need for oxygen-free conditions when
recrystallizing the salt.

4.3. REACTIONS WITH ALKYL HALIDES

The displacement of halide by cyanide in primary alkyl
halides was effected by phase transfer catalysis in studies by
Starks [4,5]. The reaction was used in this study to assess the
potential of PNP salts and to compare them with other catalysts.
(i) Phase Transfer reactions. The conditions employed by
Starks, [4] were used as a guide to begin the study although the
reactions were carried out on a much smaller scale (typically
using 10 mmol rather than 1 mol scale of Starks), thus the
isolated yields may be somewhat reduced. The reactions were
monitored using [1]H N.M.R. and I.R. spectroscopy. Product
purities were further checked by mass spectroscopy and elemental
analysis. The alkyl halide was stirred with an approximately

6M aqueous solution containing ~ 1.2 equivalents of potassium cyanide. The use of concentrated aqueous solutions is recommended to aid transfer into the organic phase, [6,7]. The reaction mixtures were heated to the desired temperature in an oil bath, at which stage the catalyst was added as a solid.

At 105°C, with one mol % of PNP chloride added to the system described above, octyl bromide was converted to octyl cyanide in 91% isolated yield. Conversion was greater than 95% after 1 hour. This compares well with hexadecyltributyl-phosphonium bromide, which under the same conditions also gives 91% isolated yield after 2 hours.

Lowering the temperature slowed the reaction considerably. With 1 mol % PNP$^+$Cl$^-$ present, the displacement proceeded to 50% completion after 8 hours at 40°C, and after 36 hours at 20°C. The percentage conversion was measured at different times by [1]H N.M.R. spectroscopy. Some experiments were also conducted with 2 mol % and 5 mol % PNP catalyst present, and although the reactions did proceed faster, the larger amount of PNP salt in the system increased the time required for work-up of the reaction. This involved adding diethyl ether to the system to precipitate all PNP$^+$ salts from the organic layer, followed by filtration, separation, and removal of the ether prior to distillation of the product.

The reaction with octyl chloride was much slower; only 20% of the halide was converted to the nitrile after 2 hours at 105°C in the presence of 1 mol % of PNP$^+$Cl$^-$.

(ii) <u>Stoichiometric reactions</u>. The simplicity of the phase transfer procedure, renders the use of pre-prepared PNP^+CN^- unnecessary for displacement reactions from simple alkyl halides, however a study of the use of PNP^+CN^- in these reactions does provide a useful comparison with the same system under phase transfer conditions as well as a comparison with some pre-prepared tetraalkylammonium cyanides. The stoichiometric reactions were carried out on a still smaller scale, typically 0.1 to 1 mmol. The stoichiometric reaction of octyl bromide with PNP^+CN^- in THF or acetonitrile gives octyl cyanide quantitatively at $20^{\circ}C$. When followed by [1]H N.M.R. resonances due to octyl cyanide appeared after one minute, the reaction proceeding to completion after approximately 45 minutes. The percentage conversions of octyl bromide to the corresponding nitrile in various solvents are summarised in <u>Table 1</u>. The values for tetrabutyl and tetraethyl ammonium cyanide from reference 8 are also shown for purposes of comparison.

<u>TABLE 1</u>. <u>Percentage conversions RBr → RCN (R = octyl)</u>

Salt	Solvent				
	THF	CH_2Cl_2	CH_3CN	C_6H_6	C_2Cl_4
PNP^+CN^-	95	80	95	0	0
$But_4N^+CN^-$	85	48	75	87	-
$Et_4N^+CN^-$	-	44	73	-	-

The reaction with octyl chloride was again much slower, proceeding to 80% completion in acetonitrile after 19 hours at 20°C. The reaction did proceed virtually to completion after several days. The figures in Table 1 show that PNP cyanide compares well with tetraalkylammonium salts in all solvents except benzene, in which PNP salts are insoluble. None of the solvents considered is an ideal universal solvent for stoichiometric or phase transfer reactions using PNP salts. The salts are also insoluble in diethyl ether and hydrocarbons. Acetonitrile is a useful solvent for stoichiometric reactions of PNP^+CN^-, although, as already noted, CH_3CN solutions of PNP cyanide are quite air sensitive, also acetonitrile cannot be used in phase transfer reactions as it is miscible with water. PNP salts are only sparingly soluble in THF, and extended reaction times were necessary to attain the 95% conversion shown in Table 1 (12 hours vs. 1 hour for other solvents). The most successfully used solvents are dichloromethane and chloroform, [9]. Chloroform suffers from its facile deprotonation to yield $^-CCl_3$ ion or dichlorocarbene. Initial experiments in dichloromethane with PNP^+CN^- gave slightly lower yields than expected, and more than one CN absorption in the I.R. spectrum. It seems likely that this is caused by reaction of PNP^+CN^- with the solvent. A search of the literature revealed that this reaction had been noted, [10], and may also explain the reduced conversions found for the tetraalkylammonium salts. The pseudo first order rate constant for the reaction of PNP^+CN^- with CH_2Cl_2 is 1.4 x 10^{-4} s^{-1}, giving a half life of 80 minutes at 25°C. Although CN^- reacts with CH_2Cl_2 much faster than some

other nucleophiles, e.g. OCN⁻ and SCN⁻, which have half lives of hundreds of hours in CH_2Cl_2, the cyanide ion appears to be especially reactive in this solvent, (vide infra).

4.3.1. Special Reactivity of PNP Cyanide in Dichloromethane

When an alkali metal salt is dissolved in water it dissociates into anions and cations. Salts of quaternary ions dissolved in solvents of low polarity however associate to a large extent to form ion pairs. Ion pairs are thermodynamically distinct species which co-exist with free ions in solution. A solution containing only ion pairs does not conduct electricity. Conductivity measurements can therefore be used to study ion pair formation, [11,12]. There are two types of ion pairs.

(1) Loose ion pairs, in which the ions are associated with each other, but are separated by their solvation shells.

(2) Contact ion pairs, in which the ions have squeezed out the solvent molecules.

Free ions and both types of ion pair can exist together in solution [11], Scheme 2.

$$\begin{array}{ccc} S & S & S \\ & Q^+ & S \ X^- \ S \\ S & S & S \end{array} \rightleftharpoons \left[\begin{array}{cc} S & S \\ S \ Q^+ \ S \ S \ X^- \ S \\ S & S \end{array}\right] \rightleftharpoons [Q^+X^-]$$

Scheme 2

In solvents with a dielectric constant lower than 10-15 almost no free ions exist, [6]. Each species has a different reactivity towards the alkyl halide; obviously free ions are

more reactive than loose ion pairs, which are in turn more reactive than contact ion pairs. Although actual reactivities are hard to determine, estimates have been made by analysis of kinetic data. Beronius estimates that the reactivity of ammonium chloride ion pairs is 10% of the reactivity of free chloride ions, [13]. Songstad found the reactivity of PNP^+NCS^- and $NCSe^-$ ion pairs to be roughly 40% of that of the free ions. The association constants K_A for some PNP salts in CH_2Cl_2 have been determined and compared with those of other cations, [14]. It was found that K_A was highly dependent on the cation, with R_4N^+ salts having K_A about twenty times greater than Ph_4As^+ salts which were themselves around twice as associated as PNP^+ salts. The low association and high solubility of Ph_4As^+ and PNP^+ salts in CH_2Cl_2 may be explained by specific interactions between the π electrons of the phenyl groups and the hydrogen atoms of the solvent, [14,15]. Thus PNP salts maximise the concentration of the more reactive free ions in dichloromethane. Due to the special solvation of the cations in dichloromethane, the association constants of PNP^+ and Ph_4As^+ salts are relatively independent of the anion, unlike tetraalkyl ammonium salts. PNP cyanide is an exception to this generality, since the association constant for PNPCN is three times lower than other PNP salts in dichloromethane. It has been suggested that this is due to stabilization of the cyanide ion in dichloromethane, [14].

The above considerations give an indication that special reactivity of PNP^+CN^- in dichloromethane may be expected. This was found to be the case in this study. The limitation of the

solvent is its reaction with PNPCN.

With regard to other solvents, referring to <u>Table 1</u>. The reasons for not using THF, benzene, ether, hydrocarbons or C_2Cl_4 have been mentioned (Section 3.3.). Acetonitrile is a useful alternative for substrates which are less reactive than dichloromethane, remembering that acetonitrile solutions of PNP^+CN^- must be protected from the air. For liquid/liquid phase transfer reactions, acetonitrile is unsuitable due to its miscibility with water.

The equilibria involved in a phase transfer system can be complex, they determine the amount of each species present in a given layer. <u>Scheme 3</u> shows the overall reaction, and the simplest mechanism.

$$K^+_{aq}CN_{aq} \ + \ RBr_{org} \ \longrightarrow \ K^+_{aq}Br^-_{aq} \ + \ RCN_{org}$$

VIA,

$$RBr \ + \ QCN \ \longrightarrow \ RCN \ + \ QBr \quad ORGANIC \ PHASE$$

$$\uparrow \qquad\qquad\qquad \downarrow$$

$$KBr \ + \ QCN \ \rightleftharpoons \ KCN \ + \ QBr \quad AQUEOUS \ PHASE$$
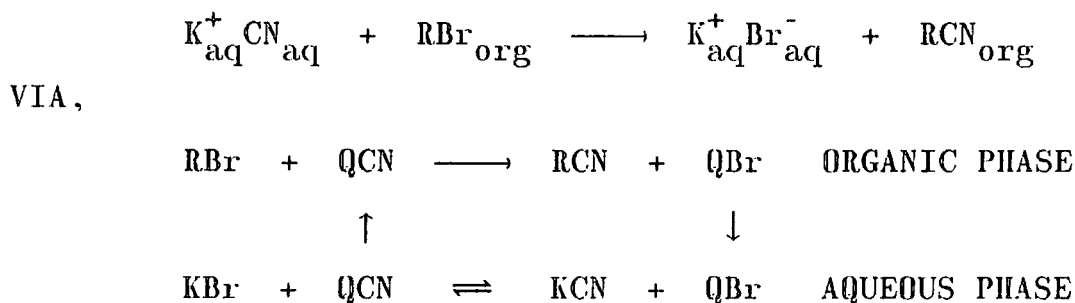
<u>Scheme 3</u>

The reaction takes place in the organic phase, between the alkyl halide and the cyanide salt, therefore knowledge of the concentration of QCN in the organic layer is desirable. This is determined by measuring extraction equilibria which describe the distribution of the salts between the layers, [6]. Makosa and co-workers determined the order of extractabilities between water and dichlorobenzene to be $Br^- > CN^- > Cl^-$ with Br^- the

most lipophilic, [16]. Thus the lower reactivity of the alkyl chloride vs. bromide appears to be entirely due to the fact that bromide is a better leaving group than chloride. Other factors which influence the extraction system include pH-dependent equilibria in the aqueous phase the formation of ion associates, $[Q^+HX_2^-]$ etc. association of ion pairs into higher aggregates, and association effects in the aqueous phase. These factors, often referred to as side reactions, depend on the cation, anion and solvent system employed. In some cases they can have a large effect and should not be neglected. For phase transfer work with PNP^+ and cyanide, using the organic substrate as the solvent is the ideal choice. Dichloromethane is the best compromise as the co-solvent if required.

4.3.2. The Reaction with Cyclohexyl Bromide

Starks reported that reaction of cyclohexyl halides with CN^- under phase transfer conditions using hexadecyltributyl-phosphonium bromide gave predominantly elimination products, [4]. 18-crown-6 was also reported to give only elimination products, [17] and no yield of cyclohexyl cyanide was recorded with t-butylamine, [18]. However Simchen reported that cyclopentyl bromide reacted with $Et_4N^+CN^-$ in acetonitrile or DMSO to give a 68% yield of the nitrile. Experiments with PNP salts under both phase transfer and stoichiometric conditions failed to produce any cyclohexyl cyanide either with or without a co-solvent. (CH_3CN, CH_2Cl_2 for the stoichiometric reaction, CH_2Cl_2 for the phase transfer.) A reaction of some nature did however take place, as an intense red/brown colour rapidly developed in the organic layer, which would become opaque after

15-20 minutes. N.M.R. and I.R. spectra revealed nothing but starting material.

Blank runs, with no PNP salts present were conducted,[†] and no colouration developed. Further investigations were not undertaken.

4.4. REACTIONS WITH ALLYL BROMIDE

This substrate can react via the usual S_N2 reaction, replacing Br with cyanide at the carbon bearing the bromine, or via vinylogous substitution which is analogous to the conjugate addition of nucleophiles to activated double bonds. This bimolecular pathway Scheme 4 is known as the S_N2' mechanism:

$$CN^- + \underset{\underset{CH_2=CH}{|}}{H_2C-Br} \xrightarrow{S_N2} CH_2=CH-CH_2CN$$

$$CN^- + CH_2=CH-CH_2Br \quad\nearrow S_N2'$$

$$CN^- + CH_2=CH-CH_2Br \xrightarrow{Rearrangement} CH_3-CH=CH-CN$$
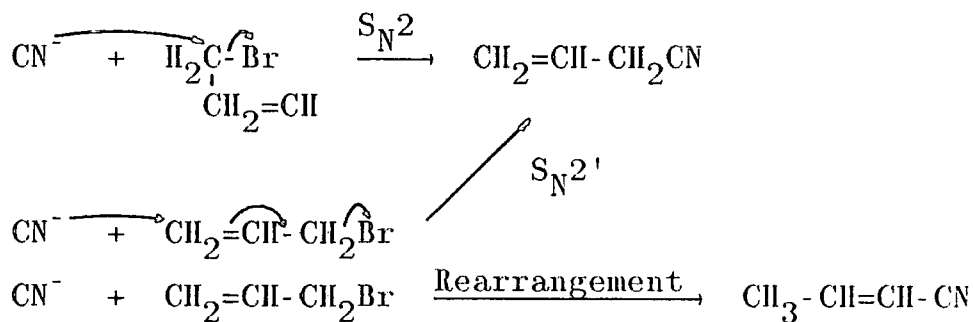
Scheme 4

it is usually slower than the S_N2 reaction, although steric hindrance may favour it. In this case S_N2 and S_N2' products are indistinguishable. A third possibility is the rearranged product formed by proton transfer in the transition state. In the presence of even small amounts of water this reaction is

[†] Such control experiments were conducted for all reactions investigated in this Chapter.

favoured and the more thermodynamically stable rearranged
product predominates. Simchen found it possible to produce a
75% yield of the S_N2 or S_N2' product after 3 hours at 0^oC using
$Et_4\overset{+}{N}CN^-$ in CH_2Cl_2. At 40^oC this was reduced to 45% of the non-
isomerised product. However the amount of rearranged product
appeared to be highly dependent on the way the reactants were
mixed as a similar reaction at 0^oC gave only 25% S_N2 or S_N2'
product, and 8% at 40^oC. No such effects were observed with PNP
salts.

The stoichiometric reaction of PNP^+CN^- with allylbromide in
CH_2Cl_2 is exothermic and proceeds to completion in under one
minute. The S_N2 or S_N2' product is the only one observed in the
^1H N.M.R. spectrum. No trace of rearranged nitrile can be
found, indicating a maximum amount of 1% $CH_3CH=CHCN$. More
remarkably the reaction can be carried out under phase transfer
conditions at 0^oC in CH_2Cl_2, using 2 mol % PNP^+Cl^- and a
concentrated aqueous solution of KCN. After one hour the
organic layer was examined by ^1H N.M.R. and I.R. spectroscopy
and found to consist of a solution of $CH_2=CH-CH_2CN$ ($\geq$ 98%). The
phase transfer conditions must protect the reaction from the
effects of the water, even though the two are in intimate
contact.

4.5. FORMATION OF ACYL NITRILES

Benzoyl cyanide was first prepared by the reaction of
benzoyl chloride with mercuric cyanide [19]. Silver or cuprous
cyanide can also be used [20,21]. Weber reported in 1974 that
aroyl cyanides could be prepared by phase transfer methods

using tetrabutyl ammonium bromide [22], however the method was limited by the formation of a dimer which is formed in 30% yield in the case of benzoyl chloride. The dimer is formed by addition of cyanide ion to the product which is trapped by unreacted starting material, Scheme 5.
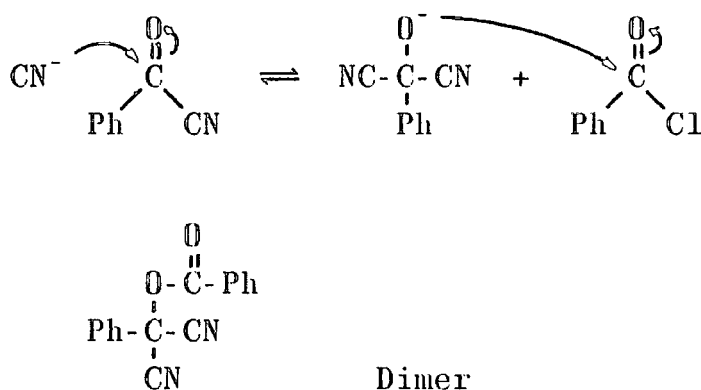
Scheme 5

The reaction is conveniently followed by I.R. spectroscopy, since the C=O absorptions of the chloride, cyanide and dimer are at 1775 cm^{-1}, 1675 cm^{-1} and 1745 cm^{-1} respectively [22]. With tetrabutylammonium cyanide the ratio of monomer to dimer was 1.7:1. Under identical phase transfer conditions, using PNP^+ (present in only 0.1 mol %), as the catalyst the monomer to dimer ratio was 6:1. Thus much less of the side product was produced. When the reaction was conducted in CH_2Cl_2 using a stoichiometric amount of PNP^+CN^-, not only was the reaction completed before the reaction mixture could be placed in the

I.R. spectrometer, but the reaction had proceeded cleanly to give only the monomeric benzoyl cyanide quantitatively. The lack of any dimer may perhaps be due to the great reactivity of PNP^+CN^- in CH_2Cl_2. All of the CN^- reacting with benzoyl chloride, leaving no CN^- to initiate reaction with the product.

This is an example of the use of homogeneous reaction conditions to alter product distributions. Even though both benzoyl chloride and benzoyl cyanide are hydrolysis-sensitive, no hydrolysis products were detected, even under phase transfer conditions.

Attempts to extend this reaction to aliphatic acyl chlorides were unsuccessful; solutions of acetylchloride in CD_3CN or CD_2Cl_2 gave complicated ^1H N.M.R. spectra containing many peaks when treated with solutions of PNP^+CN^-. However, no other ion system, catalytic or stoichiometric, has succeeded either, [9].

4.6. REACTIONS OF TRIMETHYLSILYL HALIDES

Trimethylsilyl cyanide, TMSCN is used to protect carbonyl functions in organic synthesis by formation of silylated cyano-hydrins, [23], Scheme 6.

$$Me_3SiCN \;+\; R_1\overset{\overset{O}{\|}}{C}R_2 \;\longrightarrow\; R_1\text{-}\underset{\underset{CN}{|}}{\overset{\overset{OSiMe_3}{|}}{C}}\text{-}R_2$$
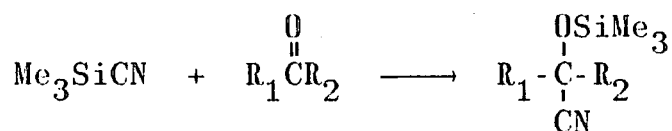
Scheme 6

TMSCN is also used for other organic transformations, [24]. Traditionally trimethylsilyl cyanide was prepared by using either expensive silver cyanide or by the use of HCN, [25]. It was reported that trimethylsilyl cyanide could not be made directly from KCN simply by heating trimethylsilyl chloride with KCN in a dipolar aprotic solvent [26]. However, Rasmussen and Heilmann proposed that TMSCN was generated in situ under such conditions in cyanosilylations of aldehydes and ketones accomplished by heating KCN, TMSCl and the carbonyl compound in a dipolar aprotic solvent such as acetonitrile or DMF, [27]. They confirmed that this was in fact the case by preparing and isolating TMSCN by heating TMSCl with KCN in N-methylpyrollidine [24]. The protection of carbonyl functions using trimethylsilyl cyanide is itself catalysed by phase transfer or stoichiometric homogeneous techniques, [23,28,29]. Trimethylsilyl compounds are notoriously prone to hydrolysis. The benefits offered by the use of PNP salts appeared to suit the above systems. Initially the preparation of TMSCN from TMSCl was attempted. It has been briefly reported that TMSCN can be made from TMSCl in 36% yield by solid/liquid phase transfer catalysis using 18-crown-6 in CH_2Cl_2, [30].

Stoichiometric reactions between PNPCN and TMSCl were attempted under various conditions, with and without solvent, (CH_2Cl_2), over a range of temperatures and reaction times. The most drastic conditions employed were to reflux neat TMSCl over PNPCN for 16 hours. No detectable TMSCN was produced. Attempts at solid/liquid phase transfer with PNPCl, solid KCN and neat or solvated TMSCl were also unsuccessful. Addition of even a trace

of water always resulted in rapid hydrolysis of the TMSCl.

Greater success was achieved with trimethylsilyl bromide, TMSBr; the 1:1 reaction of TMSBr with PNPCN in CH_2Cl_2 or $CHCl_3$ gave greater than 95% conversion to TMSCN in a few minutes. Once again control reactions with TMSBr and KCN with or without solvent failed to produce any TMSCN. Solid/liquid and liquid/liquid phase transfer experiments with TMSBr, PNPCl, and KCN gave the same non-productive reactions of the chloride.

Truesdale and co-workers described the preparation of trimethylsilyl cyanohydrins by simply heating TMSCN with carbonyls, [23]. They subsequently reported that the reaction was catalysed by the cyanide ion introduced into the organic phase with 18-crown-6, [29].

The possibility of performing the sequence of reactions in Scheme 7, i.e. the synthesis of trimethylsilyl cyanohydrins directly from TMSBr using PNPCN, or by phase transfer using PNPCl was investigated.

$$Me_3SiBr \xrightarrow{\text{PNPCN}} Me_3SiCN$$

$$R_1R_2C{=}O \ + \ CN^- \ \longrightarrow \ R_1R_2{-}\underset{\underset{CN}{|}}{C}{-}O^- \ + \ Me_3SiCN$$
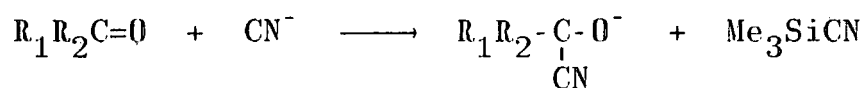
Scheme 7

The uncatalysed addition of TMSCN to cyclohexanone was reported to take place with 89% yield, [23], although no experimental details regarding temperature were given. Attempts to synthesise the cyanohydrin by simply heating cyclohexanone with TMSCN through a range of temperatures and reaction times

were unsuccessful. However when a trace of PNPCN was added to the system, the I.R. absorption of the carbonyl of cyclohexanone was considerably reduced in intensity, and the CN absorption shifted from 2195 cm^{-1} of TMSCN to 2235 cm^{-1}. Unreacted starting materials were removed in vacuo. Subsequent microdistillation yielded the trimethylsilyl cyanohydrin.

Reaction of TMSBr with a slight excess of PNPCN in the presence of cyclohexanone did not give a good yield of the silyl cyanohydrin, although I.R. spectra did indicate that it was formed. Reproducibility was poor, and isolation unsuccessful, partially due to the large amount of PNPCN required because of its high relative molecular mass compared with those of cyclohexanone and TMSBr.

Results from experiments with trimethylsilyl cyanide and benzaldehyde were also unclear, and complicated by the possible occurrence of the benzoin condensation. Further experiments with silyl cyanohydrins were not conducted.

4.7. REACTION WITH TRIMETHYLTIN CHLORIDE

Trimethyltin chloride could react with CN^- either by S_N2 reaction analogous to that of TMSBr to give trimethyltin cyanide, or by use of available d orbitals to form a pentacoordinate adduct. Stoichiometric reaction of Me_3SnCl with PNPCN gives the 1:1 adduct $[PNP]^+[Me_3SnClCN]^-$, δSn -171 ppm, δ +21 ppm. The large negative tin N.M.R. shift is characteristic of pentacoordinate anionic Sn(IV) species, [31].

4.8. THE BENZOIN CONDENSATION

Phase transferred cyanide ion can act as a catalyst. The cyanide ion transferred by crown ethers catalyses the benzoin condensation, [32], Scheme 8, and addition of 13 mol % $But_4N^+CN^-$ to a mixture of benzaldehyde and water gave a 65% yield of crude benzoin after 16 hours at room temperature. Under the same conditions, $Et_4N^+CN^-$ gave 13% crude benzoin. No benzoin was detected using sodium cyanide. Benzoin is traditionally prepared by refluxing benzaldehyde with 20 mol % NaCN in a 50% aqueous ethanol solution, [34].

$$2Ph-\underset{O}{\overset{}{\underset{\|}{C}}}-H \quad \xrightarrow[\text{catalytic}]{CN^-} \quad Ph-\underset{H}{\overset{OH}{\underset{|}{C}}}-\overset{O}{\overset{\|}{C}}-Ar$$
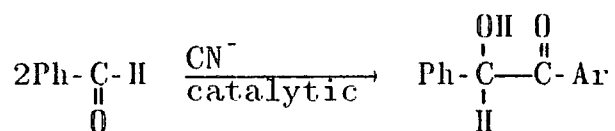
Scheme 8

PNPCN was far more efficient; 0.7 mol % of PNPCN produced a 50% yield of pure benzoin on recrystallization, after 16 hours of reaction at $20^{o}C$. The benzoin is formed as a solid lump, thus Solodars procedure of simply filtering and washing the product does not remove a great deal of the trapped starting material, or indeed the 8 g of trapped tetrabutylammonium catalyst present in a typical reaction producing 17 g of benzoin. The crude material produced after filtering and drying was further purified in this study by recrystallization from ethanol. Analysis of the mother liquor confirmed the presence of substantial quantities of PNP salts (despite the 20-fold lower concentration of PNP vs. tetrabutyl-ammonium salt) and

some trapped benzaldehyde. Thus the actual yield of pure benzoin using tetrabutylammonium cyanide is probably considerably lower than 65%.

The most spectacular results were achieved when the condensation was carried out under phase transfer conditions using PNPCl and aqueous potassium or sodium cyanide. At 40°C using 1 mol % PNPCl with a 3 mol % potassium cyanide solution, pure benzoin was isolated in 80% yield after less than 30 minutes reaction time. The yield is limited by the fact that the organic layer solidifies, trapping unreacted benzaldehyde and preventing the reaction from proceeding any further. Vigorous stirring using a magnetic or overhead stirrer improves the yield, by increasing the surface area of the solid, which forms as small pellets of around 5 mm diamater, rather than as a single solid lump. The amount of trapped starting material is decreased. With suitable stirring yields of pure benzoin in excess of 85% were obtained. The rate of reaction was increased by adding more KCN to the aqueous phase, without altering the amount of PNP salt. At 80°C the reaction was completed in around ten minutes.

4.9. CONCLUSIONS

PNPCN has been shown to be a useful reagent for effecting transformations using the cyanide ion, particularly in hydrolysis-sensitive procedures. PNPCN appears to have enhanced reactivity in dichloromethane, but its use in this solvent is limited by solvolysis. PNPCl in conjunction with a reservoir of aqueous alkali metal cyanide provides a cheaper system for such

transformations by phase transfer catalysis. Protection from

hydrolysis is more limited under phase transfer conditions.

REFERENCES

1. A. Martinsen and J. Songstad, <u>Acta Chemica. Scand. A</u>, <u>31</u>, 645 (1977).

2. J.K. Ruff and W.J. Schlientz, <u>Inorg. Synth.</u>, <u>15</u>, 84, (1974).

3. J. Songstad, Private communication (1983).

4. C.M. Starks, <u>J. Amer. Chem. Soc.</u>, <u>93</u>, 195, (1971).

5. C.M. Starks and R.M. Owens, <u>J. Amer. Chem. Soc.</u>, <u>95</u>, 3613, (1973).

6. E.V. Dehmlow and S.S. Dehmlow, "Phase Transfer Catalysis", Monographs in Modern Chemistry, <u>11</u>, Springer-Verlag, Florida, (1980).

7. Y. Sasson and H.A. Zahalka, <u>J. Chem. Soc. Chem. Commun.</u>, 1347, (1983).

8. H. Kobler, K.H. Schuster and G. Simchen, <u>Liebig. Ann. Chem.</u>, 1940, (1978).

9. W.P. Weber and G.W. Gokel, "Phase Transfer Catalysis in Organic Synthesis", Springer-Verlag, New York (1977).

10. S. Bekkevoll, I. Svorstol, H. Hoiland and J. Songstad, <u>Acta Chemica. Scand.</u>, B37, 934-45, (1983).

11. L.G. Savedoff, <u>J. Amer. Chem. Soc.</u>, <u>88</u>, 664, (1966).

12. P. Beronius and A. Brändström, <u>Acta Chemica. Scand.</u>, A30, 687-91, (1976).

13. P. Beronius, A.M. Nilsson and G. Wikander, <u>Acta Chemica. Scand.</u>, <u>24</u>, 2826, (1970).

14. I. Svorstol, H. Hoiland and J. Songstad, <u>Acta Chemica. Scand.</u>, B<u>38</u>, 885-893, (1984).

15. J. Homer and M.C. Cooke, <u>J. Chem. Soc. A</u>, 2862, (1962).

16. M. Makosa and E. Bialecka, <u>Synth. Commun.</u>, <u>6</u>, 313, (1976).

17. L.F. Cook, C.W. Bowers and C.L. Liotta, <u>J. Org. Chem.</u>, <u>39</u>, 3416 (1974).

18. W.P. Reeves and M.R. White, <u>Synth. Commun.</u>, <u>6</u>, 193, (1976).

19. Wohler and Liebig, <u>Annalen</u>, <u>3</u>, 249 (1832).

20. (a) H. Habner, <u>Annalen</u>, <u>120</u>, 330 (1861).

    (b) J.V. Nef, <u>Annalen</u>, <u>287</u>, 307 (1895).

21. T.S. Oakwood and C.A. Weisgerber, <u>Org. Synth. Coll. Vol</u>, <u>3</u>, 112, (1955).

22. K.E. Koenig and W.P. Weber, <u>Tet. Lett.</u>, <u>26</u>, 2275-78, (1974).

23. D.A. Evans, L.K. Truesdale and G.L. Carroll, <u>J. Chem. Soc. Chem. Commun.</u>, 55, (1973).

24. J.K. Rasmussen and S.M. Heilmann, <u>Synthesis</u>, 219, (1978).

25. D.A. Evans, G.L. Carroll and L.K. Truesdale, <u>J. Org. Chem.</u>, <u>39</u>, 914, (1974).

26. B. Uznanski and W.J. Stec, <u>Synthesis</u>, <u>154</u>, (1978).

27. J.K. Rasmussen and S.M. Heilmann, <u>Synthesis</u>, 523, (1979).

28. D.A. Evans and L.K. Truesdale, <u>Tet. Lett.</u>, 4929, (1973).

29. D.A. Evans, J.M. Hoffman and L.K. Truesdale, <u>J. Amer. Chem. Soc.</u>, <u>95</u>, 5822, (1973).

30. J.W. Zubrick, B.I. Dunbar and H.D. Durst, <u>Tet. Lett.</u>, 287, (1971).

31. (a) P.J. Smith and Tupciauskas, <u>Ann. Rep. N.M.R. Spectroscopy</u>, <u>8</u>, 291, (1978).

    (b) G.F. Hewitson, M.Sc. Thesis, University of Durham, (1980).

32. S. Akaboris, M. Ohtomi and K. Arai, <u>Bull. Chem. Soc Japan</u>,
     <u>49</u>, 746, (1976).

33. J. Solodar, <u>Tet. Lett</u>., 287, (1971).

34. A.I. Vogel, "A Textbook of Practical Organic Chemistry",
     4th Edition, Longman, London, 1978.

CHAPTER 5

EXPERIMENTAL

5.1. TECHNIQUES AND INSTRUMENTATION

5.1.1. Inert Atmosphere and Vacuum Line

Unless otherwise stated, all manipulations were carried out under an inert atmosphere of either nitrogen or argon. A Faircrest glovebox equipped with a catalytic oxygen removal system was used for larger manipulations. Standard Schlenk techniques were used on a vacuum/argon line equipped with drying towers of P_2O_5 and molecular sieve, bubblers to monitor gas flow, a mercury manometer for vacuum distillations and a mercury column to monitor vacuum transfers, particularly of HCN.

5.1.2. Elemental Analysis and Melting Points

Melting points were determined on a Reichert-Kofler block at atmospheric pressure and are uncorrected. Carbon, hydrogen and nitrogen analyses were obtained on a Perkin-Elmer 240 Elemental Analyser or a Carlo Erba Model 1106 analyser. Phosphorus, palladium and halogen analyses were obtained using a Perkin-Elmer atomic absorption spectrophotometer.

5.1.3. Solvents

Solvents were dried and deoxygenated prior to use by standard techniques [1].

5.1.4. N.M.R. Spectroscopy

Aldrich N.M.R. solvents were used as supplied or dried and deoxygenated as required. Proton N.M.R. spectra were obtained using a Varian EM360L spectrometer or a Hitachi-Perkin-Elmer R-24B spectrometer, both operating at 60 MHz, or a Brüker AC250 spectrometer operating at 250 MHz. Data were recorded for 16 or 32 K points. Spectra were referenced to TMS.

Carbon spectra were recorded on a Brüker AC250 operating at

63 MHz. Spectra were referenced to TMS.

Phosphorus spectra were obtained on a Perkin-Elmer R10 operating at 32 MHz, Brüker AC250 operating at 101 MHz or a Brüker WH360 operating at 145 MHz. Spectra were referenced to 85% H_3PO_4 or to TMS on an absolute chemical shift scale.

Tin spectra were recorded on a Perkin-Elmer R10 spectrometer operating at 29.7 MHz. Spectra were referenced to Me_4Sn.

The temperature of the probe was maintained within $\pm 1^0C$ using a Brüker temperature unit to control the flow of boiling liquid nitrogen or heater as required.

5.1.5. Infrared Spectroscopy

I.R. spectra were obtained using a Perkin-Elmer 580A spectrophotometer, or a Perkin-Elmer 577 spectrophotometer. Spectra of solid samples were recorded as Nujol mulls between KBr plates, or were pressed into KBr discs. Spectra of liquid samples were recorded as thin films between KBr plates.

5.1.6. Optical Rotations

Optical rotations were measured at specified concentrations in various solvents with a Perkin-Elmer 141 polarimeter, or a Thorn Automation automatic polarimeter type 243, path length 1 cm (University of Newcastle-upon-Tyne) referenced to a 1% sucrose solution at 20^0C. Measurements were made at 589 nm.

5.1.7. Chromatography

Column chromatography was performed using Merck Kieselgel 60H. Thin layer chromatography was performed using Merck plastic backed silica plates. Chromatograms were observed using u.v. irradiation or developed by iodine vapour. Preparative

thin layer chromatography was carried out using glass plates coated with silica to a depth of 2 mm, or using commercially available 20 x 20 cm Merck Kieselgel 60 F_{254} plates. Bands were identified using u.v. light.

Gas liquid chromatography was performed using a Hewlett Packard 5890A gas chromatograph fitted with a 25 m fused silica column.

5.1.8. Mass Spectrometry

Mass spectra were recorded on an AEI MS9 spectrometer or a VG 7070E spectrometer with electron impact, chemical ionization and fast atom bombardment techniques. FAB techniques are particularly suited to obtaining spectra of metal complexes [2].

5.2. THE PREPARATION AND HANDLING OF HCN

HCN is extremely toxic, it is made more dangerous by its low boiling point (27°C) and the inability of some workers to detect its smell. This project required the use of highly pure HCN in accurately measured quantities, for use in the laboratory on a day to day basis. The development of safe efficient handling techniques was called for, the methods used are described below.

5.2.1. Detection of HCN

In order to ensure that all pieces of apparatus (reaction vessels, vacuum line etc.) were free of HCN after use, a method of detecting HCN is desirable. Early workers recommended that a cigar be smoked when working with HCN, as the presence of HCN could be detected by a change in the taste of the cigar smoke, this method was not used in this study however. An HCN

detection system marketed by Gastek was used.

Air to be sampled is drawn through a tube containing mercury(II) chloride and methyl orange. HCN displaces chloride from the mercury(II) chloride. The liberated HCl is detected by the indicator which turns red. This reaction is used for HCN concentrations in the range 2.5 to 120 ppm, concentrations of 0.05 to 2% HCN were measured with 'high range tubes' containing yellow potassium palladsulphite which reacts with HCN to form a white compound. This reaction formula is still unknown.

5.2.2. Preparation of HCN

HCN was prepared in the laboratory by dropping glacial acetic acid onto high quality KCN [3]. Mineral acids give unwanted polymeric by-products. HCN was collected from the preparation by connecting the reaction vessel to a cold trap with polythene tubing. (HCN attacks rubber tubing.) This method was used to prepare 5-10 mls of HCN at a time. The purity of the gas was checked by I.R. in a gas cell at 10 cmHg pressure of HCN.

I.R. Spectrum literature, [4].

cm^{-1} 712.1 vs. 1412.0 ‖ s 2116.7 m 2800.3 s 3312.0 ‖ s
found 712 vs. 1412 s   2110 w   2800 s   3312 s

The liquid was stored over a little solid P_2O_5 which maintains the liquid in anhydrous form; the phosphoric acid formed inhibits polymerization.

5.2.3. Stabilization

Pure liquid HCN is liable to flash polymerize, this is a highly exothermic, often explosive process, therefore pure HCN must be maintained below $0^{\circ}C$ at all times. Industrial samples

of HCN, which were used towards the end of this project are stabilized with SO_2, however this gas deactivates transition metal catalysts. A typical analysis of the industrial samples of HCN obtained from W.R. Grace was 0.1% phosphoric acid, 0.1% H_2O, 281 ppm SO_2. Prior to use the HCN was placed in an ice cooled beaker, then purged with nitrogen for 3 to 5 minutes. The liquid was then transferred to sealable glass 'rotaflo' vessels containing ~ 10 mg P_2O_5 per 5 ml HCN. The HCN was distilled from the 'rotaflo' when required, to give pure anhydrous HCN, which was subsequently maintained below $0^{o}C$.

5.2.4. Measurement of HCN

(i) For hydrocyanation reactions. A typical reaction used 300-500 mg of HCN, however, if the ligand was expensive, or if the ligand or substrate was in short supply, the techniques described below will measure, and deliver to a reaction, amounts of HCN of around 100 mg with an accuracy of about ±5%. The method is based on a simple vacuum transfer with precautions to maintain the liquid below $0^{o}C$. The vacuum line was first cleaned and greased. Leaks were tested for by taking the line down to vacuum, the pump was isolated and the level of the 76 cm mercury column manometer was observed over $\frac{1}{2}$ hour.

The first step was to remove nitrogen or air from the HCN storage rotaflo, so that when connected to the distillation, the manometer would only measure the pressure of HCN in the line. This was simply done by freezing the HCN in the bottom of the rotaflo with an isopropanol/CO_2 bath, evacuating the rotaflo, then closing its tap. The storage rotaflo was left connected to the line and allowed to warm up to $0^{o}C$ in an ice bath. All

vessels were connected directly to the line by short glass adapters, as HCN interacts with rubber, leading to inaccurate transfer and contaminated tubing. A second, small (30 ml), rotaflo was evacuated on the line, then its tap was closed, and after removal from the line, the grease was washed off it with chloroform. The rotaflo was thus weighed empty, then reconnected to the line after re-greasing. The pump was isolated, and the small rotaflo, (having been opened to the line before the pump was isolated), was cooled in the isopropanol/CO_2 bath. The storage rotaflo was tipped sideways to give the maximum surface area of HCN. The tap of the storage rotaflo was opened carefully to admit HCN to the line and the small rotaflo. The HCN was transferred in portions, never allowing the pressure of HCN in the line above ~ 20 cmHg. The surface of the HCN often froze over, when this occurred, the tap of the storage rotaflo was closed and the HCN remelted by gently warming the tube by hand. If this was not done, the liquid HCN below the frozen surface would 'bump' and throw lumps of solid HCN into the line, which were very slow to remelt and evaporate due to the lack of conduction mechanisms. When sufficient HCN appeared to have been collected, the taps on both rotaflos were closed and the line re-opened to the vacuum pump. The line was then filled with nitrogen and the rotaflos removed. Before the amount of HCN transferred was determined by weighing, the rotaflos were placed in the fridge for five minutes in order to prevent the HCN boiling on the walls of the rotaflo when it was weighed. Condensed water on the outside of the rotaflo was wiped away prior to weighing, this was repeated until a constant

reading was obtained, then the rotaflo was returned to an ice/salt bath next to the balance. If the amount of HCN collected was incorrect, then the above procedure was repeated. transferring HCN from one rotaflo to the other until the required amount of HCN was obtained.

(ii) <u>For N.M.R. tube scale reactions</u>. The N.M.R. scale experiments required the addition of known quantities of HCN in the region of 10-30 μl to solutions of metal complexes in N.M.R. tubes to examine the products by ^{1}H and ^{31}P N.M.R. To achieve this, a rotaflo of HCN and a microlitre syringe of the appropriate volume were chilled in the freezer, meanwhile about 400 ml of acetone in a glass dish, wrapped with aluminium foil were cooled to -20°C with dry ice. The above items, together with the N.M.R. sample were transferred to a glove box. The HCN was allowed to liquify in the box, and measured into the N.M.R. tube using the microlitre syringe. The HCN was then quickly re-solidified in the acetone bath. The sample in the N.M.R. tube was sometimes cooled briefly prior to HCN addition to prevent loss by evaporation prior to sealing the tube, however cooling was kept to a minimum to avoid pressure build-up when the thin walled N.M.R. tubes were warmed to room temperature.

(iii) <u>Other methods</u>. Measurement of HCN by volume, condensing HCN into a graduated vessel on the vacuum line, proved less accurate than the weighing technique described in (i). The ideal method of HCN addition and measurement would have been to add HCN gradually, as high concentrations of HCN are undesirable in hydrocyanation reactions as noted above. One such method would be to pass nitrogen over liquid HCN, then into

the reaction vessel. This method requires a regulated flow of nitrogen, and some intricate calibration experiments. The added complication of the high reaction temperature led to the abandonment of the method.

A technique was developed to achieve gradual HCN addition using calibrated syringe drives, but was only suitable for relatively large HCN feed rates (ml min^{-1}).

5.2.5. Disposal of HCN

The destruction of unreacted or unwanted HCN was initially carried out by extracting reaction mixtures with sodium hydroxide. The sodium cyanide formed was then disposed of using a commercial preparation of hypochlorite solution, ("chloros") which contained an exhaustion indicator. This solution was frozen into the low temperature traps of the vacuum line whenever HCN was handled on the line.

The use of sodium hydroxide was quickly discontinued as it introduced extra manipulations into small scale reactions. Unreacted HCN was subsequently removed by distillation and the fraction disposed of by igniting it. HCN burns in a similar manner to ethanol, with a gentle blue flame. Disposal of HCN by combustion in a fume cupboard is a simple safe efficient technique and was used to dispose of quantities of up to 800 ml of HCN.

5.3. EXPERIMENTAL FOR CHAPTER TWO

5.3.1. Reagents

Reagents supplied by the Aldrich Chemical Company were used without further purification unless otherwise stated.

Palladium(0)bisdibenzylideneacetone was recrystallized as a solvate from benzene [5]. Nickel and palladium triphenylphosphite complexes were prepared by literature methods [6,7], as was vinyl acetamide, [8] and bisbenzonitrile palladium dichloride, [9]. Vinyl acetate was distilled under nitrogen prior to use to remove added stabilizers.

5.3.2. Preparation of Diphenylmenthylphosphinite

A solution of chlorodiphenylphosphine (14.62 g, 66 mmol) in THF (300 ml) was cooled to -5°C. Menthol (10.37 g, 66 mmol) and triethylamine (13 g, 132 mmol) were dissolved in THF (100 ml) and this solution was added to the chlorophosphine dropwise with stirring over two hours. The temperature was maintained between -5 and 0°C. Approximately one quarter of the solvent was then removed under reduced pressure, the ice bath was removed and the mixture was stirred for a further five hours. The gelatinous white reaction mixture was filtered through 'hyflosupercel' filter aid on a sinter. The solvent was removed to leave a viscous oil, which was redissolved in THF (50 ml) and filtered again. This process was repeated until all traces of the amine salt had gone. The remaining oil was left to crystallize overnight at 5°C. Yield 21.6 g (96%) m.p. 34-36°C.

Analysis Found C 78.0% H 8.53% P 8.9%

$\quad\quad\quad$ $C_{22}H_{20}OP$ requires C 77.6% H 8.5% P 9.1%.

[1]H N.M.R. (60 MHz, CDCl$_3$), δ7.3 (M, 20H, OP(C$_6$H$_5$)$_2$, δ3.6 (m, 1H CHOPPh$_2$), δ2.3-0.5 ppm (m, 18H, alkyl protons).

[13]C N.M.R. (CDCl$_3$), δ131-128 (phenyl carbons), δ81.6 C-OPPh$_2$, δ49.6, δ45.8, δ43.8, δ34.6, δ32.0, δ25.6, δ23.2, δ22.5, δ21.4, δ15.8 ppm, (alkyl carbons).

[31]P N.M.R. (CDCl$_3$), δ106.0(s).

I.R. P-O-C stretch 1017 cm^{-1}, aromatic CH stretch, 3050 cm^{-1}.

5.3.3. Preparation of 1-1'-Bi-2-napthylbis(diphenylphosphite)

Binapthol (1.98 g, 6.93 mmol) was dissolved in pyridine, (18 ml) to give a very dark brown suspension. A solution of chlorodiphenylphosphine, (3.1 g, 14 mmol) in pyridine, (15 ml) was added dropwise with stirring. After addition of 2-3 ml the suspension became a brown solution. Once all the phosphine had been added the mixture was warmed to 45°C for three hours. A further 1.5 g (7 mmol) of the phosphine were added after cooling, then the mixture was heated to 45°C for a further three hours. The mixture was cooled to 0°C and the precipitated pyridinium hydrochloride was removed by filtration and washed with pyridine (2 x 3 ml). The pyridine was removed in vacuo (0.01 mmHg, 45°C) and the remaining brown solid was washed with hexane (8 x 30 ml), to give, on drying, a pale sand powder, (3.8 g, 84%), m.p. 187°C, lit. [10], 170-171°C.

Analysis Found C 79.6% H 4.98% P 9.2%.

$C_{44}H_{32}O_2P_2$ requires C 80.7% H 4.9% P 9.5%

I.R., no OH stretch.

[31]P N.M.R. δ111.0(s).

5.3.4. Preparation of N-tert-Butoxycarbonyl-2S,4S-4-(diphenyl-phosphino)-2-[(diphenylphosphino)methyl]pyrrolide (BPPM)

All steps in the preparation were conducted using literature methods, [11,12], apart from those in the following sections.

5.3.5. Preparation of 4-Hydroxy-ℓ-proline Ethyl Ester Hydrochloride

To a slurry of 4-hydroxy-ℓ-proline, (25 g, 380 mmol) in absolute ethanol (300 ml) was carefully added acetyl chloride (55 ml, 760 mmol) in portions. After the initial heat of reaction had subsided, the mixture was heated to reflux, becoming homogeneous after two hours. The reaction mixture was heated for a further eight hours, then allowed to cool to $5^{o}C$. The white needle-like crystals which formed were washed with diethyl ether (3 x 100 ml) and dried in vacuo to give the ester hydrochloride (34 g, 91%), m.p. $142^{o}C$ (lit. [12], $153^{o}C$, $147^{o}C$).

[1]H N.M.R. (250 MHz, Me_2SO d_6), $\delta 9.7$ (br.s., 2H, $N\underline{H}_2^{+}$), $\delta 4.21$ (q, 2H, J = 7 Hz $-CO_2C\underline{H}_2CH_3$), $\delta 1.25$ (t, 3H, J = 7 Hz $-CO_2CH_2C\underline{H}_3$) ppm.

I.R. (Nujol mull) 1735 cm^{-1} (C=O str), 3320 cm^{-1} (OH stretch).

5.3.6. Preparation of N-(tert-Butoxycarbonyl)-4-Hydroxy-ℓ-proline Ethyl Ester

(i) Using Di-t-butyl dicarbonate. A suspension of 4-hydroxyproline ethyl ester hydrochloride, (8 g, 41 mmol) in CH_2Cl_2 (20 ml) containing triethylamine (8 ml, 100 mmol) was cooled to $-5^{o}C$ under argon. Di-t-butylcarbonate, (18.5 g, 82 mmol) was added to the solution, followed by 4-dimethylamino-pyridine, (5.2 g, 42 mmol), which was added in portions with stirring. The mixture was stirred at room temperature for 15 hours to give a bright yellow solution. The solvent was removed under reduced pressure to give a solid which was washed with dilute hydrochloric acid (2 x 100 ml; 0.2M). The residue was taken up into hexane (300 ml), and washed first with

hydrochloric acid, (2 x 50 ml, 0.1M), then with sodium bicarbonate until effervescence ceased (~ 80 ml, 0.05M). The extract was finally washed with water, (5 x 100 ml), then dried over anhydrous magnesium sulphate. The hexane was removed under reduced pressure (80°C, 10 mmHg) to give the product as a colourless oil (8.5 g, 80%).

^{1}H N.M.R. (60 MHz, CDCl$_3$) δ4.21, (q, 2H, J = 7 Hz, CO$_2$CH$_2$CH$_3$), δ2.4-δ2.0, (m, 3H, OHCH$_2$) δ1.43 (s, 9H, CO$_2$C(CH$_3$)$_3$), δ1.25 ppm (t, 3H, J = 7 Hz, CO$_2$CH$_2$CH$_3$).

I.R. (neat) 1700-1740 cm^{-1} (C=O stretch), 3460 cm^{-1} (OH stretch).

(ii) Using 2-t-butoxycarbonyloxyimino-2-phenyl acetonitrile (BOCPhCN). To a solution of 4-hydroxyproline ethyl ester hydrochloride, (5 g, 25 mmol) in water (15 ml), and triethylamine (10 ml), was added dioxan (15 ml) and BOCPhCN (7 g, 28 mmol). The mixture was stirred under argon for 5 hours. Water (35 ml) and ethylacetate (50 ml) were added, the aqueous layer was removed and extracted with ethyl acetate (2 x 30 ml). The combined extracts were washed with dilute NaOH, (2 x 60 ml, 0.25M), dilute HCl, (1 x 30 ml, 0.01M) and water (3 x 30 ml). The extract was dried over anhydrous magnesium sulphate to give the product as a pale yellow oil, (6.3 g, 95%), with identical N.M.R. and I.R. spectral parameters as the material from method (i).

(iii) Using t-butoxycarbonyl azide. A solution containing 4-hydroxyproline ethyl ester hydrochloride (42 g, 214 mmol), t-butoxycarbonyl azide, (52 ml, 226 mmol) and triethylamine (63 ml) in dioxan/water (210 ml/210 ml) was heated and stirred at

50°C under N_2 for 15 hours. The mixture was reduced in volume by half on a rotary evaporator, then extracted with ether, (4 x 40 ml). The combined ether extracts were washed with brine, dried over magnesium sulphate, filtered and the ether removed. The resulting yellow oil, (41 g, 75%) was maintained at 0.05 mmHg, 20°C for 24 hours, the material was indistinguishable by I.R. or N.M.R. from samples prepared by routes (i) or (ii); and was used without further purification.

5.3.7.   Preparation of N-t-Butoxycarbonyl-2S,4S)-4-(diphenyl-
         phosphino)-2-[(diphenylphosphino)methyl]pyrrolidine
         (BPPM)

Potassium (2.34 g, 60 mmol) and sodium metal (0.6 g, 25 mmol) were melted together in a Schlenk under argon. A solution of triphenylphosphine, (8 g, 30 mmol) in dioxan (100 ml) was added by steel cannula and the mixture was stirred vigorously for 3 hours. To the resultant orange suspension was added, over ten minutes, a cooled solution of N-(t-Butoxycarbonyl)-4-hydroxy-ℓ-proline-di-p-toluenesulphonate (7.87 g, 15 mmol) in toluene, (40 ml). The solution was stirred under argon for 15 hours, then filtered through a small plug of celite over two hours. The remaining cake was washed with warm toluene (2 x 30 ml) over 2 hours. The solvent was removed from the filtrate to leave a brown oil. The oil was cautiously treated with methanol at -78°C, discharging the brown colouration to give a pale yellow slurry at room temperature. The solvent was removed after filtration to give a pale yellow oil which was taken up into a minimum volume of warm ethanol. After a week to ten days at 5°C, white crystals began to form, these were separated by

filtration, washed with a little ethanol and dried in vacuo, the material was slightly yellow and could be further purified by recrystallization to give white crystals. Yield of 1st crystals (4.7 g, 57%). Literature values are from reference [12].

Analysis Found C 71.6 H 6.60 N 2.33

$C_{34}H_{37}NO_2P_2$ requires C 73.44, H 6.73, N 2.41.

I.R. (KBr disc) 622, 660, 676, 690, 1368, 1450, 1600, 1690
(C=O stretch) lit. 620, 658, 672, 685, 1360, 1450, 1600, 1690 cm^{-1}.

^{1}H N.M.R. (250 MHz $CDCl_3$), $\delta 7.6-7.2$, (m, 20H, Ph_2P), $\delta 3.78$, (m, 2H, $H^cH^{f'}$), $\delta 3.11$ (dt $J_{ff'} = J_{PCCH}f = 11$ Hz, $J_{ef} = 8$ Hz, 1H, H^f), $\delta 2.90-2.65$, (m, 2H, H^b, H^e), $\delta 2.3-1.7$, (m, 3H, $H^{b'}$, H^d, $H^{d'}$), $\delta 1.32$, (s, 9H, H_a).
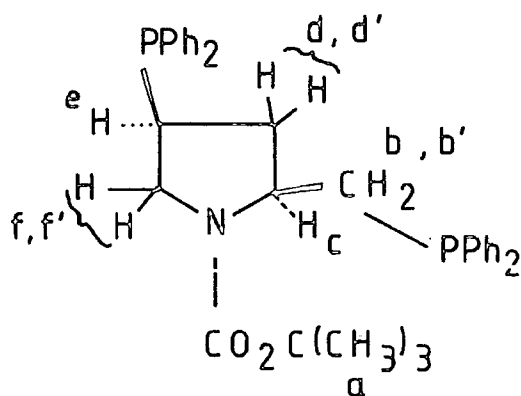
^{13}C N.M.R. ($CDCl_3$) 21.4, 27.7, 33.5, 34.1, 52.0, 52.4, 54.2, 69.4, 69.7, 78.3, 78.9, 80.2, 125.3, 127.6, 129.8, 132.4, 133.3, 145.0, 154.0 ppm.

lit. 21.2, 28.0, 33.62, 35.2, 51.4, 53.4, 68.4, 79.0, 125.4, 127.6, 130.2, 131.1, 142.4, 150.8 ppm.

[31]P N.M.R (CDCl$_3$)   318K δ-21 (s, 1P), δ-6.8 (s, 1P)

300K δ-21 (s, 1P), δ-7.2, -6.6 (1P) ppm

$[\alpha]_D^{20}$ (C = 0.4, C$_6$H$_6$), -23^0 (lit. -23^0).

5.3.8. Preparation of Dichlorobisdiphenylmenthylphosphinite Palladium(II)

DPMPH (506 mg, 1.488 mmol) were dissolved in benzene, (7 ml), the solution was added by steel cannula to a cooled, stirred solution of dichlorobisbenzonitrile palladium(II) (383 mg, 0.74 mmol) in benzene, (10 ml). The orange colour of the solution was immediately discharged to give a clear solution. Stirring was discontinued after three hours. Unlike other L$_2$PdCl$_2$ complexes the (DPMPH)PdCl$_2$ did not precipitate on adding petroleum ether, (25 ml), even after prolonged refrigeration, therefore all the solvent was removed in vacuo. The canary yellow solid was dissolved in a minimum volume of warm benzene, addition of petroleum ether caused the precipitation of a pale yellow solid which was collected by filtration and dried (0.01 mmHg, 5 hrs.). Yield 310 mg, 50%. m.p. 180-3^{0}C (dec).

Analysis   Found C 61.9%   H 7.8%

C$_{48}$H$_{58}$O$_2$P$_2$PdCl$_2$ requires C 61.5%   H 6.7%.

[31]P N.M.R. (CD$_2$Cl$_2$) δ100 (s) δ98 (s).

Mass Spectrum, (FAB) in thiodiglycol. L$_2$Pd 786 with palladium isotope pattern.

5.3.9. Typical Hydrocyanation Reaction

A carius tube (100 ml) was charged with bisdibenzylide acetone palladium(0), (13.6 mg, 0.0236 mmol), BPPM, (112 mg, 0.203 mmol), the tube was evacuated and let down to argon, through a cone to tap adapter. A dried filtered benzene

solution, (5 ml) of norbornene (2.68 g, 28.52 mmol) was added by syringe through the inlet bore of the stopcock tap. A further 7 ml of benzene was used to wash the reactants away from the neck of the tube. The adapter was removed and the carius tube was attached directly to the vacuum line. The contents were solidified by cooling to $-78^{\circ}C$ in an isopropanol NO_2 bath. The carius tube was then evacuated, the pump isolated and hydrogen cyanide (385 mg, 14.26 mmol) was distilled into the carius tube. The tube was sealed under vacuum, then allowed to warm to room temperature. The solution changed from the wine red colour of bisdibenzylidene acetone palladium(0) to the pale green colour of free bisdibenzylidene acetone. The homogeneous solution was heated to $120^{\circ}C$ for 18 hours, then opened. The contents were poured into a 25 ml round bottom flask and the unreacted HCN, norbornene and benzene were removed by distillation at atmospheric pressure. The remaining liquid was transferred to a microdistillation apparatus and a fraction was collected b.p. $80^{\circ}C$, 6 mmHg. The fraction solidified to a white waxy solid (1.175 g, 68%), identical to authentic exo norbornane carbonitrile, [9]. The enantiomeric purity of the products was measured according to section 5.7.

5.3.10. Hydrocyanation of Vinyl Acetate

Triphenylphosphite (1.96 g, 6.3 mmol) and distilled vinyl acetate (2.16 g, 25 mmol) were syringed into a carius tube under nitrogen. Palladium(0)tetrakistriphenylphosphite (250 mg, 0.18 mmol) was dissolved in benzene (5 ml) and the solution was filtered through cotton wool into the carius tube. Benzene (7 ml) was used to wash the reactants into the lower part of the

carius tube, which was cooled to -78°C. HCN (0.34 g, 12.5 mmol) was condensed into the tube, which was sealed and heated to 120°C for 18 hours.

After opening, the mixture was distilled at atmospheric pressure to remove benzene and unreacted vinyl acetate. The residue was transferred to a microdistillation apparatus and the fraction collected of boiling range 65-70°C (water pump pressure). Lit., [13], Yield (1.14 g, 81%).

^{1}H N.M.R. (250 MHz, CDCl$_3$) δ5.36 (q, 1H, C-$\underline{H}$, J_{CH,CH_3} = 6.6 Hz), δ2.13, (s, 3H, OCH$_3$), δ1.6 (d, 3H, C$\underline{H}_3$, J_{CH,CH_3}= 6.6 Hz).

Mass Spectrum CI 131 M + NH$_4$$^+$.

5.3.11. Typical Small Scale Hydrocyanation

The initial procedure was the same as for BPPM, using dipalladiumtrisdibenzylideneacetone benzene (40 mg, 0.04 mmol), BINAP, (233 mg, 0.37 mmol), norbornane, (2.9 g, 30 mmol), benzene (12 ml) and HCN, (416 mg, 15.4 mmol).

The reaction solution was homogeneous before the reaction, changing from orange to pale green after heating to 120°C for 18 hours. Unreacted norbornene, HCN and benzene was removed by distillation. The residue was too small to allow conventional microdistillation. The material was therefore treated with hexane to precipitate the phosphine, filtered and the hexane was removed on a rotary evaporator. The remaining solid was placed in a small Schlenk, to which was fitted a CO$_2$/isopropanol cooled 'bucket'. The Schlenk was evacuated and the outside warmed with a water bath (80°C). The waxy solid was collected and identified as pure exo-norbornane carbonitrile by comparison with an authentic sample. Yield 111 mg, 6%. $[\alpha]_D^{20}$ -11^0 (C =

0.91, CHCl$_3$), corresponding to a 40% enantiomeric excess.

5.3.12. The Use of Acetone Cyanohydrin for Hydrocyanations

The process of charging a carius tube with reactants, particularly HCN, then cracking the tube to recover the products is time consuming and potentially hazardous. An attractive alternative appeared to be the use of acetone cyanohydrin in place of HCN. Using the cyanohydrin, reactions could be carried out in refluxing toluene in a flask, and could be worked up straight from the flask. Jackson and co-workers reported no loss of preparative or optical yield using this technique in place of HCN in sealed vessels, [9]. Other workers have reported adverse effects on yields when acetone cyanohydrin was substituted for HCN, [14]. The catalyst systems of interest in this study are the same as, or similar to those used by Jackson, therefore it was considered advantageous for some time to use acetone cyanohydrin in toluene in place of HCN. However the work-up of reactions was cleaner and simpler using HCN in benzene as both are volatile and are easily removed by distillation at atmospheric pressure. Unreacted acetone cyanohydrin b.p. 82°C, 25 mmHg was difficult to remove, and its boiling point is close to many of the products of interest, therefore the use of acetone cyanohydrin was discontinued.

5.3.13. Derivatisation of Norbornane Carbonitrile for
Determination of Enantiomeric Composition

Norbornane carbonitrile, (224 mg, 1.6 mmol) were stirred at 40°C for 2 hours with concentrated HCl, (1.2 ml). Distilled water (1.2 ml) was added and the mixture was refluxed for 12 hours. The cooled solution was extracted with ether (2 x 20

ml). The combined extracts were dried ($MgSO_4$), filtered, and the ether was removed to give a waxy solid which was sublimed at $60°C$ 0.01 mmHg to give the product (153 mg, 58%).

m.p. $56°C$ lit. [9] $56-58°C$.

__I.R.__ 1695 cm^{-1}, (C=O stretch), 3100, (OH stretch).

^{1}H __N.M.R.__ (60 MHz, $CDCl_3$) δ11.0, (br s, 1H, COO__H__), δ2.55, (br s, 1H, H1), δ2.5-2.1, (m, 2H, H2,4), δ2.00-1.05 (m, 8H, H3,5,6,7).

5.3.14. __Preparation of (S) Norbornane Carboxylic Acid-Methyl__
        __Mandelate Ester__

To a solution of norbornane carboxylic acid (140 mg, 1.0 mmol) in dichloromethane (5 ml) at $-10°C$ was added 4-dimethylaminopyridine (2.5 mg), followed by (S)Methyl-2-hydroxy-2-phenylethanoate (166 mg, 1.0 mmol) and dicyclohexylcarbodiimide (206 mg, 1.0 mmol) the mixture was stirred for three hours. The heavy white precipitate of urea was removed by filtration. The solvent was removed under reduced pressure. The residue was taken up in dichloromethane (2 ml), filtered again and the solvent removed under reduced pressure.

A preliminary thin layer chromatogram (silica 5:1, hexane/ethyl acetate) showed two components Rf 0.27-0.36 and Rf 0.73. The remaining material was purified by preparative thin layer chromatography on two 20 x 20 cm silica plates. The band corresponding to the ester was removed from the plates and the product isolated by extraction with diethyl ether followed by removal of the solvent in vacuo. (The remaining material was dissolved in benzene d$_6$ and used directly for the ^{1}H N.M.R.

measurements described in Chapter 2.)

^{1}H N.M.R. (250 MHz, C_6D_6), δ7.5-7.2, (m, 5H, ArH), δ6.5, (2s, 1H, CH), δ3.2 (s, 3H, CH_3), δ2.7-2.6 (2brs, 1H, H1), δ2.4-δ1.0 ppm (10H, H2,3,4,5,6,7).

5.3.15. Preparation of Bis BPPM Nickel(0)

$NiCl_2 \cdot 6H_2O$ (28.5 mg, 0.12 mmol) and BPPM, (135 mg, 0.24 mmol) were dissolved in ethanol (5 ml) and water (1 ml). A solution of sodium borohydride, (13.5 mg, 0.36 mmol) in water was added dropwise over five minutes to the cooled stirred solution. A bright yellow precipitate formed which was too fine to separate by filtration. The solution was removed by steel cannula and the precipitate was washed with ethanol (2 x 2 ml) and dried (0.01 mmHg) to give a bright yellow solid, (35 mg, 25%).

I.R. (KBr disc) 1685 cm^{-1} ($\nu_{C=0}$).

^{31}P N.M.R. (C_7H_8) 298K δP 23.3, 23.9, 24.7, 25.0, 26.8.

5.4. EXPERIMENTAL FOR CHAPTER 3

5.4.1. Reagents were used as supplied by the Aldrich Chemical Company or the Sigma Chemical Company and were used without further purification. Bis(trimethylacetonitrile)platinum(II)-dichloride and some (DIOP) platinum(0) ethene was kindly supplied by Dr. Richard Taylor.

5.4.2. Preparation of (DIOP) Palladium(0) Ethene

Into a solution of (DIOP) palladium dichloride, (160 mg, 0.24 mmol) in dry ethanol (1.5 ml) and dichloromethane (3.7 ml), cooled to -78°C was passed ethene gas (15 minutes). To the solution was added a freshly prepared cold solution ($\sim$ -30°C) of

sodium borohydride, (22 mg, 0.6 mmol) in ethanol (2.5 ml) over a period of five minutes, maintaining the ethene atmosphere throughout. The mixture was allowed to warm slowly to room temperature, the colour of the solution changed from an opaque white to red and finally brown over a period of about twenty minutes. Highly reflective crystals began to form as the ethene flow was maintained. After two hours the supernatant liquid was removed by syringe and the colourless crystals were washed with cold ethene saturated ethanol (3 x 1 cm^3). The crystals were dried in vacuo (0.01 mmHg), and were stored at -15°C under ethene as a precaution (104 mg, 69%). m.p. 80°C (dec).

Analysis Found C 63.0%, H 5.38%, Cl Absent, P 10.0%, Pd 16.8%.

$C_{33}H_{36}O_2P_2Pd$ requires C 62.6%, H 5.69%, P 9.8%, Pd 16.8%.

^{1}H N.M.R. (250 MHz, CD_2Cl_2) δ7.8-7.2 (m, 20H, Ar), δ3.98 (m, 2H, CHO), δ3.07 (m, 2H, CHP), δ2.83 (m, 2H, olefin CH), δ2.59 (m, 2H, olefin CH), δ2.36 (dd, 2H, CHP), δ1.3 (s, 6H, CMe$_2$) ppm.

^{31}P N.M.R. (CD_2Cl_2) +6.8 ppm.

Supplementary X-ray Data

TABLE 1. Dihedral Angles Between Planes

Plane No.	Atoms in Plane		
1	Pd	C1	C2
2	Pd	P1	P2

Dihedral angle between planes

Plane No.	Plane No.	Dihedral Angle
1	2	5.8

TABLE 2

Summary of Crystal Data and Details of Intensity Collection

compound	$(diop)PdC_2H_4$
fw	633.00
formula	$C_{33}H_{36}PdO_2P_2$
space group	$P2_1$
Z	2
cell parameters	a,Å = 10.664(3) β = 109.41(2)^0
	b,Å = 11.023(4)
	c,Å = 13.926(2)
	V,Å^3 = 1543.9
ρ(calcd.), gcm^{-3}	1.36
temp, ^{0}C	23
radiatn.	MoK$_\alpha$ (λ = 0.71073Å, graphite monochromated)
take-off angle, deg.	2.8
scan rate, deg/min	from 1 to 3 (in ω)
scan width, deg.	0.6 + 0.350 tanθ
maximum 2θ, deg.	54
μ, cm^{-1}	7.2
unique data collected	3549
unique data used ($F_0^2 > 3\sigma (R_0^2)$)	2220
final no. of parameters refined	342
error in observation of unit weight	1.16
R	0.034
R$_w$	0.037

TABLE 3

Final Fractional Coordinates for Non-Hydrogen Atoms with Estimated Standard Deviations in Parentheses

Atom	x	y	z	B(A2)
Pd	0.11790(4)	0.25*	0.23417(3)	3.652(8)
P1	0.1627(2)	0.0717(2)	0.3234(1)	3.56(4)
P2	-0.0935(2)	0.3043(2)	0.2236(1)	3.67(4)
O1	-0.0688(5)	0.0081(5)	0.4886(4)	6.7(1)
O2	-0.2065(4)	0.1684(5)	0.4505(3)	4.6(1)
C1	0.1874(8)	0.3770(8)	0.1489(5)	6.1(2)
C2	0.2870(7)	0.2967(9)	0.1943(5)	6.2(2)
C3	0.0252(6)	0.0013(6)	0.3554(5)	4.1(2)
C4	-0.0265(6)	0.0823(7)	0.4230(5)	4.0(2)
C5	-0.1495(6)	0.1603(6)	0.3730(4)	3.4(1)
C6	-0.1311(6)	0.2891(6)	0.3430(4)	4.0(2)
C7	-0.1864(6)	0.0563(8)	0.5008(5)	5.3(2)
C8	-0.1630(8)	0.0791(12)	0.6117(6)	9.0(3)
C9	-0.2992(11)	-0.0267(11)	0.4538(9)	10.3(3)
C11	0.2147(6)	-0.0471(7)	0.2529(5)	4.0(2)
C12	0.1399(8)	-0.1460(9)	0.2089(6)	6.7(2)
C13	0.1889(9)	-0.2287(8)	0.1552(6)	7.9(3)
C14	0.3083(8)	-0.2122(9)	0.1441(5)	7.3(2)
C15	0.3820(7)	-0.1181(9)	0.1866(6)	6.7(2)
C16	0.3378(7)	-0.0339(9)	0.2420(6)	5.8(2)
C21	0.2947(6)	0.0640(7)	0.4471(5)	4.0(2)
C22	0.3241(7)	-0.0404(8)	0.5031(6)	5.7(2)

Continued

Positional Parameters and Their Estimated Standard Deviations
(cont.)

C23	0.4210(8)	-0.0405(10)	0.5991(6)	7.1(2)
C24	0.4894(8)	0.0611(10)	0.6380(6)	6.8(2)
C25	0.4644(8)	0.1653(9)	0.5813(7)	7.0(2)
C26	0.3679(7)	0.1674(7)	0.4838(6)	5.1(2)
C31	-0.2315(6)	0.2185(5)	0.1366(4)	3.6(2)
C32	-0.3627(6)	0.2508(12)	0.1197(5)	5.2(2)
C33	-0.4650(7)	0.1779(10)	0.0612(6)	6.8(2)
C34	-0.4395(7)	0.0739(8)	0.0173(6)	6.0(2)
C35	-0.3135(8)	0.0436(7)	0.0323(5)	5.7(2)
C36	-0.2067(7)	0.1141(7)	0.0914(5)	5.0(2)
C41	-0.1436(6)	0.4612(6)	0.1865(5)	4.3(2)
C42	-0.1361(9)	0.5000(8)	0.0947(7)	6.7(2)
C43	-0.1640(10)	0.6176(9)	0.0621(8)	9.2(3)
C44	-0.2012(10)	0.6989(8)	0.1228(9)	10.9(4)
C45	-0.2088(10)	0.6617(9)	0.2093(10)	9.5(4)
C46	-0.1823(8)	0.5429(7)	0.2449(7)	6.2(2)

Anisotropically refined atoms are given in the form of the
isotropic equivalent thermal parameter defined as:

$$4/3 \left[a^2 B_{11} + b^2 B_{22} + c^2 B_{33} + ab\cos\gamma B_{12} + ac\cos\beta B_{13} + bc\cos B_{23} \right]$$

* The y-coordinate of Pd was fixed to define the origin.
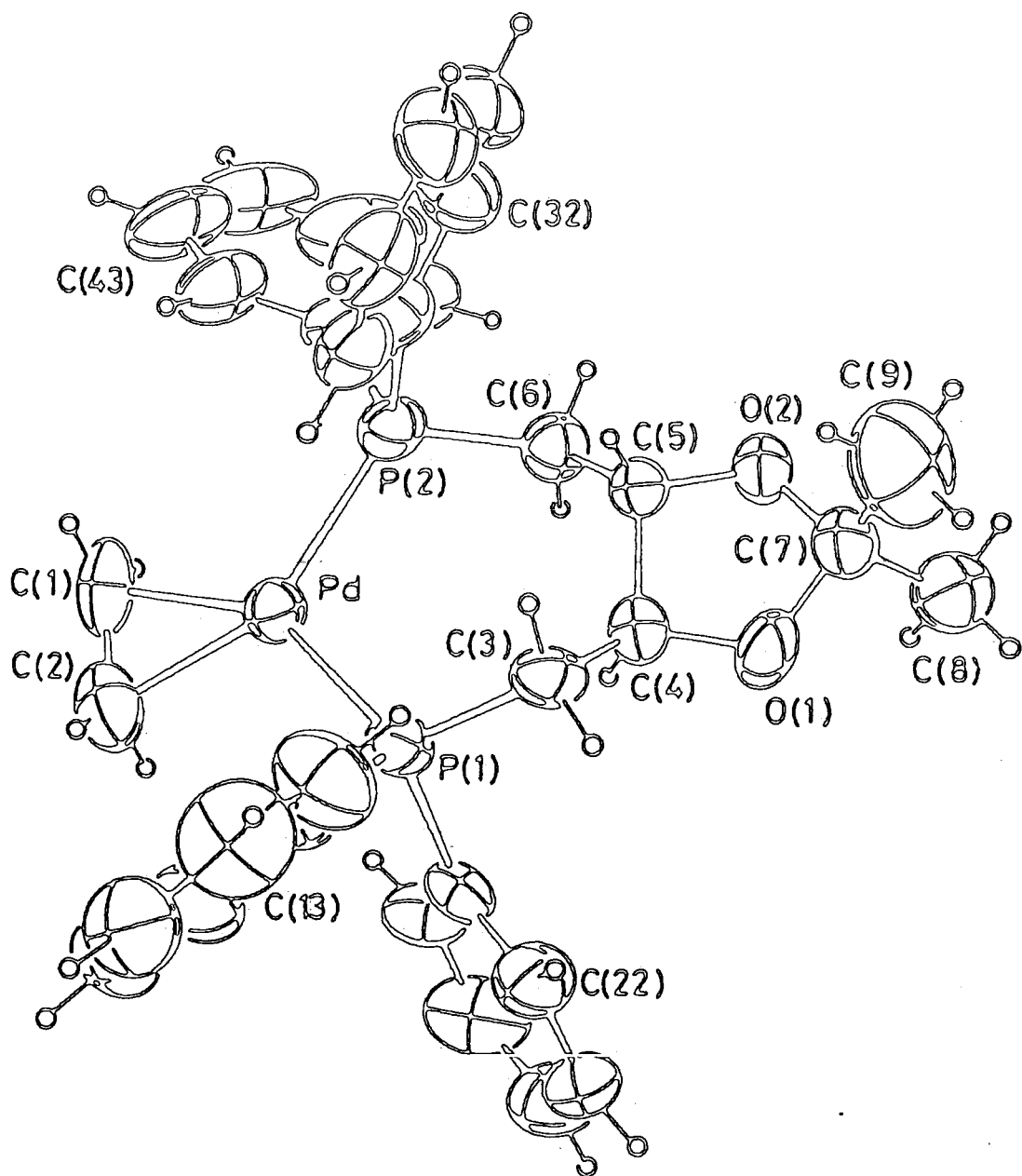
Figure 1. Molecular structure   ; key dimensions Pd–C(2)
2.119(8), Pd–C(1) 2.122(8). C(1)–C(2) 1.366(11), Pd–P(1), Pd–P(2)
2.289(2) Å; P(2)–Pd–P(1) 106.4, C(1)–Pd–C(2) 37.6(3), Pd–C(1)–
C(2) 71.1, P(1)–Pd–C(1) 145.2, P(1)–Pd–C(2) 108°.

5.4.3. Reactions of (DIOP) Palladium Ethene

To a solution of (DIOP) palladium ethene (12 mg, 19 μmol) in THF (2 ml) was added a solution of the substrate (20-50 μmol) in THF (2 ml). The mixture was stirred for ten minutes, and then the solvent and ethene were removed under reduced pressure. Alternatively the derivatisations were performed in situ by direct addition of the substrate to a solution of (DIOP) palladium ethene in d^8 toluene or dideuterodichloromethane in an N.M.R. tube.

Products

(i) (DIOP)Pd norbornene δP (CD$_2$Cl$_2$) 6.2 ppm.

(ii) (DIOP)Pd(-carvone) δP (C$_6$D$_6$) P$_a$ 7.3, P$_b$ 4.3 ppm, J$_{PaPb}$ 40 Hz.

(iii) (DIOP)Pd TCNE δP (CD$_2$Cl$_2$) 8.8 ppm.

(iv) (DIOP)Pd(H)CN δP (CD$_2$Cl$_2$) 4.0, P$_b$ -6.3, J$_{PaPb}$ 13 Hz ^{1}H N.M.R. (250 MHz, CD$_2$Cl$_2$) δ-4.9 ppm (Pd-H).

(v) (DIOP)Pd-η^3-allyl acetate δP (CD$_2$Cl$_2$) 8.1 ppm.

(vi) (DIOP)Pd(η^1-allyl)Cl δP (CD$_2$Cl$_2$) P$_a$ 20.8 ppm, P$_b$ 2.0 ppm, J$_{PaPb}$ 40 Hz.

(vii) (DIOP)Pd(Ph)I δP (CD$_2$Cl$_2$) P$_a$ 13.2, P$_b$ -3.2, J$_{PaPb}$ 41 Hz.

5.4.4. Preparation of (DIOP) Platinum Cl$_2$

To a solution of bis(trimethylacetonitrile)dichloro-platinum(II), (120 mg, 0.28 mmol) in dichloromethane, (5 ml) was added a solution of DIOP (137 mg, 0.28 mmol) in dichloromethane (5 ml). After stirring for fifteen minutes the product was precipitated by the addition of methanol. After filtration, the product was washed with cold methanol (2 x 1 ml) and dried.

5.4.5. Preparation of (DIOP) Platinum Ethene

To a solution of (DIOP) platinum dichloride (200 mg, 0.26 mmol) in dichloromethane (5 cm^3) and ethanol (4 cm^3) at -78°C was added a solution of sodium borohydride (24.5 mg, 0.65 mmol) in ethanol, (2 ml). The addition and subsequent reaction was carried out under a flow of ethene gas. The mixture was stirred at -78°C for twenty minutes, then allowed to warm up to room temperature. The mixture was transferred by steel cannula into ethanol (30 cm^3). After 15 minutes the product was collected by filtration (116 mg, 62%).

^{1}H N.M.R. (CD$_2$Cl$_2$, 250 MHz), δ7.7-7.2, (m, 20H, Ar), δ3.95-3.91, (m, 2H, C$\underline{H}$O), δ3.65-3.42 (m, 2H, CH$_{a\ or\ b}$P), δ2.45-2.35 (m, 2H, CH$_{a\ or\ b}$P), δ2.1-2.0, (m, 2H, J$_{PtH}$ 57 Hz, CH$_2$), δ1.85-1.8 (m, 2H, J$_{PtH}$ 57 Hz CH$_2$), δ1.3 ppm (s, 6H, CMe$_2$).

^{31}P N.M.R. (CD$_2$Cl$_2$) δP 13.7 ppm, J$_{PPt}$ 3585 Hz.

5.4.6. Reactions of (DIOP) Platinum Ethene

Derivatisations were carried out as for (DIOP) palladium ethene (section 5.4.3.).

Products

(i) (DIOP)Pt(norbornene)

^{1}H N.M.R. (250 MHz, C$_7$D$_8$) δH 8.0-7.2 (m, 20H, Ar), 4.25, (m, 2H, CHO), 3.7 (m, 2H, CH$_{a\ or\ b}$P), 3.0, (2H, bridgehead CH), 2.9 (m, 1H, olefinic bound CH), 2.75 (m, 1H, olefinic bound CH), 2.60 (m, 2H, dd with Pt satellites, ^{3}J$_{PtH}$ 20 Hz, CH$_{a\ or\ b}$P), δ1.60 (m, 2H, bridge CH$_2$), δ1.3 (s, 6H, CMe$_2$), δ1.00 (m, 4H, CH$_2$CH$_2$).
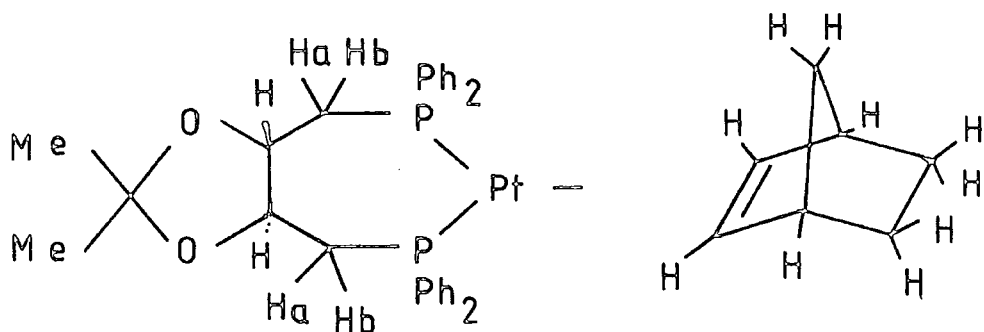
^{31}P N.M.R. (C$_7$D$_8$) δP 15.8 ppm, J$_{PPt}$ 3414 Hz.

(ii) (DIOP) Pt(norbornadiene)

^{1}H N.M.R. (250 MHz, C$_7$D$_8$) δH, 8.0-7.2 (m, 20H, Ar), 6.86 (m,

1H, free olefinic H$_{1a \text{ or } b}$), 6.74 (m, 1H, 'free' olefinic H$_{1a}$

$_{\text{or } b}$), 4.23 (m, 2H, CHO), 3.75 (m, 2H, CH$_{a \text{ or } b}$P), 3.45 (m,

2H, H$_2$), 3.29 (m, 1H, bound olefinic H$_{3a \text{ or } b}$), 3.25 (m, 1H,

bound olefinic H$_{3a \text{ or } b}$), 2.55 (m, 2H, CH$_{a \text{ or } b}$P), 2.28 (m, 2H

bridge H),, 1.45 (s, 6H, CMe$_2$).
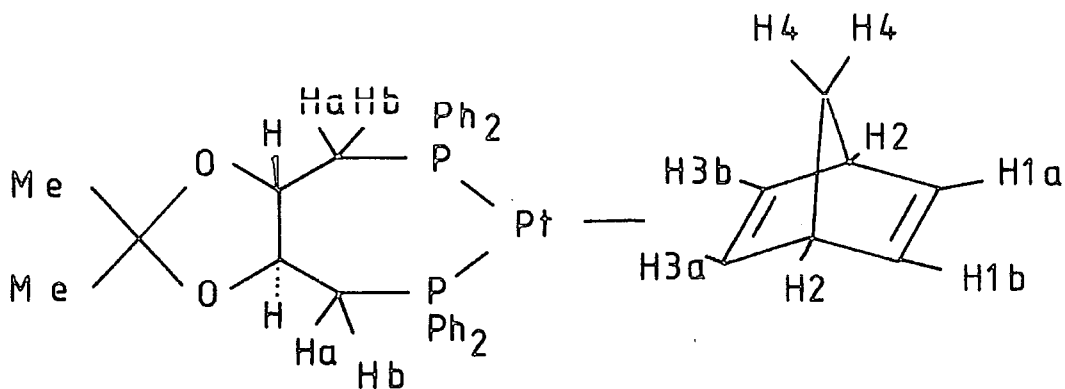
^{31}P N.M.R. (C$_7$D$_8$) δP 14.6 ppm, J$_{PPt}$ 3251 Hz.

(iii) (DIOP) Pt(H)CN

^{1}H N.M.R. (250 MHz, C$_7$D$_8$), δ-4.02 ppm (PtH), J$_{HPt}$ 967 Hz, J$_{HP}$

187 Hz trans, 16 Hz cis.

[31]P N.M.R. (C_7D_8) δP P_a 5.35, P_b 4.1, J_{PtPa} 2840 Hz, J_{PtPb} 1725 Hz, J_{PP} 17 Hz.

5.4.7. Preparation of (BPPM) Palladium(II) Dichloride

A solution of BPPM, (236 mg, 0.427 mmol) in benzene, (5 ml) was added by steel cannula to a stirred filtered solution of bisbenzonitrile palladium(II) dichloride, (163 mg, 0.427 mmol) in benzene (5 ml). After two to three minutes, a white precipitate began to form, stirring was discontinued after twenty minutes. Petroleum ether (boiling range 30-40°, 7 ml) was added to precipitate the product, which was collected by filtration and washed with petroleum ether, (2 x 5 ml). The product was a pale cream solid (225 mg, 70%).

Analysis Found C 55.74%, H 4.97%, N 1.89%, Pd 15.22%, Cl 9.65%.

$C_{34}H_{37}NCl_2O_2P_2Pd$ requires C 55.89%, H 5.06%, N 1.92%, Pd 14.52%, Cl 9.73 %.

$[\alpha]_D^{20}$ -72.3° (C = 0.7 CHCl$_3$).

[1]H N.M.R. (250 MHz, CD_2Cl_2), δ7.7-7.2 (m, 20H, Ar), δ4.0-1.6 (8H, aliphatic BPPM protons), δ1.38 (s, 9H, CMe$_3$).

[31]P N.M.R. (217K, CD_2Cl_2) δP_a 43.1, 42.8 (d, 1P, J_{PP} = 10 Hz), δP_b 25.4, 23.7 (d, 1P, J_{PP} = 10 Hz).

I.R. (KBr disc) 1690 cm^{-1} ($\nu_{C=0}$).

5.4.8. Preparation of Bis BPPM Palladium(0)

(BPPM) palladium(II) dichloride, (152 mg, 0.21 mmol) and BPPM (115 mg, 0.21 mmol) were dissolved in acetone (8 ml) to give a pale yellow solution. The solution was cooled in ice and a solution of sodium borohydride (34 mg, 0.8 mmol) in water (1 ml) was added dropwise with stirring over five minutes. The

precipitated yellow solid was filtered, washed with cold methanol (3 x 5 ml) and dried. Yield (122 mg, 48%).

$[\alpha]_D^{20}$ -30.5 (C = 0.6, CHCl$_3$).

^{1}H N.M.R. (250 MHz, CD$_2$Cl$_2$) δ7.7-7.2 (m, 20H, Ar), δ4.0-1.6 (m, 8H, aliphatic BPPM protons), δ1.30 (s, 9H, CMe$_3$).

^{31}P N.M.R. (250 MHz, CD$_2$Cl$_2$) δP P$_a$ 36.0 ppm, P$_b$ -3.3 ppm, J_{PaPb} 20 Hz.

5.4.9. Preparation of (BPPM) Platinum(II) Dichloride

To a solution of BPPM (150 mg, 0.27 mmol), in benzene (8 ml) was added a suspension of bis(trimethylacetonitrile) platinum(II) dichloride (117 mg, 0.27 mmol) by steel cannula. The resulting solution was warmed to 85°C for five minutes and then stirred under nitrogen for a further two hours. The white precipitate was collected by filtration. Addition of hexane (10 ml) to the remaining solution caused further precipitation which was again collected by filtration. Yield (152 mg, 67%).

^{31}P N.M.R. (298K, CDCl$_3$) δP$_a$ 25.9, 25.4 ppm (d, 1P, J$_{PP}$, 18 Hz), δP$_b$ 2.0, 0.4 ppm (d, 1P, J$_{PP}$ 18 Hz), J$_{PaPt}$ = J$_{PPbPt}$ = 3556 Hz, J$_{Pb1Pt}$ = 3475 Hz, ^{1}J$_{Pb2Pt}$ = 3488 Hz.

5.4.10. Preparation of (BPPM) Platinum Ethene

To a solution of (BPPM)PtCl$_2$ (130 mg, 0.16 mmol) in ethene saturated ethanol (1 ml) and CH$_2$Cl$_2$ (1½ ml) at -78°C, was added a cooled solution of sodium borohydride (12 mg, 0.31 mmol) in ethanol (2 ml). The addition was carried out dropwise under a steady flow of ethene, which was maintained during the course of the reaction. After stirring at -78°C for twenty minutes, the solution was allowed to warm up to room temperature over two hours. The solvent was removed in vacuo and the remaining solid

was washed with ethanol (2 x 3 ml) and dried (0.01 mmHg). Yield (77 mg, 62%).

^{31}P N.M.R. (C$_7$D$_8$) δP$_a$ 51.0 ppm, δP$_b$ 9.3 ppm, J$_{PaPt}$ 3682 Hz, J$_{PbPt}$ 3255 Hz.

5.5. EXPERIMENTAL FOR CHAPTER FOUR

5.5.1. Reagents were used as supplied by the Aldrich Chemical Company. Allyl bromide and cyclohexanone were distilled prior to use.

5.5.2. Preparation of PNP Chloride

To a stirred solution of triphenylphosphine, (157 g, 0.6 moles) in 1,1,2,2-tetrachloroethane, (200 mls) at -25°C, chlorine, (28 g, 0.4 moles) was slowly added. After chlorine addition was finished, hydroxylamine hydrochloride, (14 g, 0.20 moles) was added to the viscous solution, which was refluxed for 8 hours, after which time HCl evolution had ceased. On cooling the solution was poured into ethyl acetate, (800 ml) and left to crystallise for 24 hours. The product was dissolved in hot toluene and filtered while cold to remove 1,1,2,2-tetrachloro-ethane and triphenylphosphine oxide. After crystallization from hot water the pH of the aqueous solution of the product was adjusted to 7.1 with NaOH to remove any traces of the hydrochloride. The crystals obtained were dried under vacuum for 4 hours. Yield 98.6 g, 86%. m.p. 275°C lit. [15], 273°C.

Analysis Found C 75.5%, H 5.5%, N 2.26%, Cl 5.91%, P 10.33%.

$C_{36}H_{30}NP_2Cl$ requires C 75.5%, H 5.26, N 2.44%, Cl 6.19%, P 10.81%.

5.5.3. Preparation of PNP Cyanide

To a solution of PNP$^+$Cl$^-$, (4.6 g, 8 mmol), in warm methanol, (50 ml), was added a solution of potassium cyanide, (0.58 g, 9 mmol), in methanol (5 cm^3) under a nitrogen atmosphere. After stirring for ten minutes the mixture was left at 0^{0}C for 3 hours, then the precipitate of potassium chloride was removed by filtration. The above process was repeated with 0.2 g, 3 mmol of potassium cyanide in methanol (5 cm^3), to ensure complete conversion. The methanol was removed in vacuo and the solid was dissolved in warm degassed acetone (15 ml) under nitrogen. Dry degassed diethyl ether was added until the stirred solution became faintly cloudy, (20-25 ml). The mixture was cooled to -10^{0}C overnight, protected from the air. The crystals were collected by filtration under nitrogen, washed with diethyl ether, (2 x 5 ml) and dried, (0.01 mmHg, 8 hours, 70^{0}C). Yield 2.1 g, 46%. m.p. 213-4^{0}C, lit. [16], 212^{0}C.

Analysis Found, C 78.5%, H 5.7%, N 4.83%, P 10.32%, Cl Absent.

$C_{37}H_{30}N_2P_2$ requires C 78.7%, H 5.35%, N 5.00%, P 10.99%, Cl Absent.

5.5.4. Preparation of Octyl Cyanide

To 1-bromo-octane, (5.0 g, 26 mmol) and PNP$^+$Cl$^-$, (0.3 g, 0.52 mmol) was added a solution of potassium cyanide, (2.0 g, 31 mmol) in water, (5 ml). The mixture was heated at 105^{0}C for two hours. After cooling, the organic layer was separated and washed with water, (2 x 15 ml). Diethyl ether, (15 ml), was added to precipitate PNP salts, which were removed by filtration. The organic layer was dried, (MgSO$_4$), the ether was removed and the residue was distilled under reduced pressure to

give a colourless liquid (3.26 g, 91%), b.p. 45-6°, 0.04 mmHg, lit., 55°, 1 mm, [17].

5.5.5. Preparation of Allyl Cyanide

To a solution of allyl bromide, (700 mg, 5.8 mmol) in dichloromethane, (5 ml) at 0°C was added a cooled solution of PNP^{+}CN^{-}, (3.67 g, 6.5 mmol) in dichloromethane, (20 cm^{3}). The solution was stirred for five minutes. Diethyl ether was added and the PNP salts were removed by filtration. The residue remaining after removal of the solvent was distilled under reduced pressure to give a colourless liquid, (370 mg, 95%). b.p. 118-9°C lit., [18], 119°C.

^{1}H N.M.R. (60 MHz, CDCl$_{3}$) δ5.8-δ5.2 (m, 3H, vinylic CH), δ3.2, (d, 2H, CH$_{2}$CN).

5.5.6. Preparation of Benzoyl Cyanide

(i) By phase transfer. Benzoyl chloride, (25.5 g, 0.18 mmol) and PNP^{+}Cl^{-}, (89 mg, 0.15 mmol) were dissolved in dichloromethane, (150 ml) and the solution was cooled to 0°C. A solution of potassium cyanide, (12 g, 0.18 mmol) in water, (10 cm^{3}), was added and the mixture was stirred for 16 hours, when infrared analysis of $\nu_{C=O}$ indicated that the reaction was complete. The organic layer was dried over anhydrous magnesium sulphate, the solvent was removed under reduced pressure and the residue was distilled under vacuum to give a colourless liquid, (12.6 g, 46%), b.p. 30°C, 0.035 mmHg, m.p. 30-32°C, lit. 30-32°C [19]. $\nu_{C=O}$ 1675 cm^{-1} lit. 1675 cm^{-1}. The distillation residue was dissolved in warm ethanol, (100 ml), treated with charcoal, filtered and cooled to yield a colourless solid, (3.56 g, 15%) m.p. 95-6°C lit., m.p. 96°C).

(ii) <u>By stoichiometric reaction with PNPCN</u>. To a solution of PNPCN, (2.82 g, 5 mmol) in dichloromethane (25 ml) was added a solution of benzoyl chloride, (702 mg, 5 mmol) in dichloromethane, (10 ml). The mixture was stirred at -10°C for 5 minutes, after which time I.R. analysis showed only the carbonyl stretch of benzoyl cyanide ($\nu_{C=O}$, 1675 cm^{-1}). The volume was reduced to 15 ml and diethyl ether was added. The precipitate was filtered off. The residue from the removal of the solvent was distilled under vacuum to give a colourless liquid, (600 mg, 92%). Identical with authentic benzoyl cyanide.

5.5.7. <u>Preparation of Trimethylsilyl Cyanide</u>

Trimethylsilyl bromide, (250 mg, 1.63 mmol) was added by syringe under nitrogen to anhydrous PNPCN, (920 mg, 1.63 mmol) and the mixture was stirred at 20°C for one hour. Diethyl ether was added, (5 ml) and the mixture was filtered. The solvent was removed under vacuum to give a colourless liquid, (150 mg, 93%), b.p. 116-7°C lit. [20] 114-117°C, $\nu_{C\equiv N}$ 2183 cm^{-1}.

$\underline{^1H\ N.M.R.}$ (250 MHz, CDCl$_3$), δ0.23 ppm.

5.5.8. <u>Preparation of Cyclohexanetrimethylsilyl Cyanohydrin</u>

To cyclohexanone, (280 mg, 2.85 mmol) was added by syringe trimethylsilylcyanide, (311 mg, 3.14 mmol). The mixture was stirred at 0°C. Solid PNPCN, (15 mg, 25 μmol) was added and the mixture was stirred at room temperature for 8 hours. I.R. analysis of the mixture showed that the carbonyl peak was greatly reduced and that ν_{CN} had shifted from 2183 cm^{-1} to 2235 cm^{-1}. Unreacted starting materials were removed under reduced pressure. The residue was distilled directly under vacuum,

(0.05 mmHg 75°C bath temperature) to give a colourless liquid, 421 mg, 75%.

I.R. (neat) 2235, 1246, 838, 750 cm^{-1} lit. [21], 1246, 838, 750 cm^{-1}.

^{1}H N.M.R. CDCl$_3$, δ0.18 (s, 9H, CH$_3$) lit. [21], CCl$_4$ δ0.15 ppm.

5.5.9. Preparation of PNP Trimethylchlorocyanostannate

To a solution of trimethyltin chloride, (108 mg, 0.54 mmol), in dichloromethane, (5 ml) was added a solution of PNPCN, (308 mg, 0.55 mmol), in dichloromethane (5 ml). Examination of the ^{119}Sn and ^{31}P N.M.R. revealed a single resonance in each case, δ^{119}Sn, -117, δ^{31}P, 21 ppm.

5.5.10. Preparation of Benzoin

To a solution of PNPCl (1.98 g, 3.28 mmol) in water (100 ml) was added KCN, (600 mg, 9.21 mmol). Benzaldehyde (25 ml, 0.246 moles) was added by syringe. The solution was stirred at 40°C for twenty minutes. Solid began to appear after ten minutes. The crude solid was recrystallized from ethanol (240 ml) to give pure white needle-like crystals of benzoin (16 g, 70%). m.p. 136°C lit. 137°C [1(b)].

REFERENCES

1. (a) A.J. Gordon and R.A. Ford, "The Chemists Companion",
    Wiley Interscience, Toronto, (1972).

    (b) A.I. Vogel, "Textbook of Practical Organic Chemistry",
    Longman, London and New York, (1978).

2. R. Davis, I.F. Groves, J.L.A. Durrant, J. Organomet. Chem.,
    241, C27-30, (1983).

3. A. Platt, Ph.D. Thesis, University of Durham, (1980).

4. G. Herzberg, "Molecular Spectra and Molecular Structure,
    II. Infrared and Raman Spectra of Polyatomic Molecules",
    D. Van Nostrand, London, (1945).

5. T. Ukai, H. Kawazura and Y. Ishii, J. Organomet. Chem., 65,
    253-266, (1974).

6. J.J. Levison and S.D. Robinson, Inorg. Synth., 13, 105,
    (1972).

7. L. Malatesta and M. Angoletta, J. Chem. Soc., 1186-88,
    (1957).

8. D.J. Dawson and R.D. Gless, J. Amer. Chem. Soc., 98, 5996,
    (1976).

9. W.R. Jackson and P.S. Elmes, Aust. J. Chem., 35, 2041-51,
    (1982).

10. R.H. Grubbs and R.A. De Vries, Tet. Lett., 1879-80, (1977).

11. I. Ojima, T. Kogure and N. Yoda, J. Org. Chem., 45,
    4728-39, (1980).

12. G.L. Baker, S.J. Fritschel, J.R. Stille and J.K. Stille, J.
    Org. Chem., 46, 2954-2960, (1981).

13. Boil., 3, 499.

14. W.C. Drinkard, U.S. Pat., 3,655,723, (1972).

15. J.K. Ruff and W.J. Schlientz, <u>Inorg. Synth.</u>, <u>15</u>, 84, (1974).

16. A. Martinsen and J. Songstad, <u>Acta Chemica. Scand.</u>, A<u>31</u>, 645, (1977).

17. <u>Beil.</u>, 2, 354.

18. <u>Beil.</u>, 2,408.

19. K.E. Koenig and W.P. Weber, <u>Tet. Lett.</u>, <u>26</u>, 2275-78, (1974).

20. Aldrich Catalogue Handbook of Fine Chemicals, Aldrich Chemical Company Ltd. (1988).

21. D.A. Evans, G.L. Carroll and L.K. Truesdale, <u>J. Org. Chem.</u>, <u>39</u>, 914-7, (1974).

APPENDIX

(1) RESEARCH COLLOQUIA, SEMINARS AND LECTURES ORGANISED BY DURHAM UNIVERSITY 1983-1986

* Denotes lecture attended.

5.10.83*   Prof. J.P. Maier (Basel, Switzerland)
               "Recent Approaches to Spectroscopic
               Characterization of Cations"

12.10.83*   Dr. C.W. McLeland (Port Elizabeth, Australia)
               "Cyclization of Aryl Alcohols through the Inter-
               mediacy of Alkoxy Radicals and Aryl Radical
               Cations"

19.10.83   Dr. N.W. Alcock (Warwick)
               "Aryl Tellurium (IV) Compounds, Patterns of Primary
               and Secondary Bonding"

26.10.83   Dr. R.H. Friend (Cavendish, Cambridge)
               "Electronic Properties of Conjugated Polymers"

30.11.83   Prof. I.M.G. Cowie (Stirling)
               "Molecular Interpretation of Non-relaxation
               Processes in Polymer Glasses"

2.12.83*   Dr. G.M. Brooke (Durham)
               "The Fate of the Ortho-fluorine in 3,3-sigmatropic
               Reactions Involving Polyfluoro-aryl and -hetero-
               aryl Systems"

14.12.83   Prof. R.J. Donovan (Edinburgh)
               "Chemical and Physical Processes Involving the
               Ion-pair States of the Halogen Molecules"

10.1.84   Prof. R. Hester (York)
               "Nanosecond Laser Spectroscopy of Reaction
               Intermediates"

18.1.84*   Prof. R.K. Harris (U.E.A)
               "Multi-nuclear Solid State Magnetic Resonance"

8.2.84*   Dr. B.T. Heaton (Kent)
               "Multi-nuclear NMR Studies"

15.2.84   Dr. R.M. Paton (Edinburgh)
               "Heterocyclic Syntheses Using Nitrile Sulphides"

7.3.84   Dr. R.T. Walker (Birmingham)
               "Synthesis and Biological Properties of some
               5-substituted Uracic Derivatives; Yet Another
               Example of Serendipity in Anti-viral Chemotherapy"

21.3.84   Dr. P. Sherwood (Newcastle)
"X-ray Photoelectron Spectroscopic Studies of Electrode and Other Surfaces"

21.3.84*   Dr. G. Beamson (Durham/Kratos)
"EXAFS: General Principles and Applications"

23.3.84   Dr. A. Ceulemans (Leuven)
"The Development of Field-type Models of the Bonding in Molecular Clusters"

2.4.84   Prof. K. O'Driscoll (Waterloo)
"Chain Ending Reactions in Free Radical Polymerisation"

3.4.84   Prof. C.H. Rochester (Dundee)
"Infrared Studies of Adsorption at the Solid-liquid Interface"

25.4.84   Dr. R.M. Acheson (Biochemistry, Oxford)
"Some Heterocyclic Detective Stories"

27.4.84   Dr. T. Albright (Houston, U.S.A.)
"Sigmatropic Rearrangements in Organometallic Chemistry"

14.5.84   Prof. W.R. Dolbier (Florida, U.S.A)
"Cycloaddition Reactions of Fluorinated Allenes"

16.5.84   Dr. P.J. Garratt (UCL)
"Synthesis with Dilithiated Vicinal Diesters and Carboximides"

22.5.84   Prof. F.C. de Schryver (Leuven)
"The Use of Luminescence in the Study of Micellar Aggregates" and
"Configurational and Conformational Control in Excited State Complex Formation"

23.5.84   Prof. M. Tada (Waseda, Japan)
Photochemistry of Dicyanopyrazine Derivatives"

31.5.84*   Dr. A. Haaland (Oslo)
"Electron Diffraction Studies of some Organo-metallic Compounds"

11.6.84*   Dr. J.B. Street (IBM, California)
"Conducting Polymers Derived from Pyrroles"

19.9.84   Dr. C. Brown (IBM, California)
"New Superbase Reactions with Organic Compounds"

21.9.84*   Dr. H.W. Gibson (Signal UOP, Illinois)
"Isomerization of Polyacetylene"

19.10.84   Dr. A. Germain (Languedoc, Montpellier)
"Anodic Oxidation of Perfluoro Organic Compounds in Perfluoroalkane Sulphonic Acids"

24.10.84*   Prof. R.K. Harris (Durham)
"N.M.R. of Solid Polymers"

28.10.84*   Dr. R. Snaith (Strathclyde)
"Exploring Lithium Chemistry: Novel Structures, Bonding and Reagents"

7.11.84   Prof. W.W. Porterfield (Hampden-Sydney College, U.S.A)
"There is no Borane Chemistry (only Geometry)"

7.11.84   Dr. H.S. Munro (Durham)
"New Information from ESCA Data"

21.11.84*   Mr. N. Everall (Durham)
"Picosecond Pulsed Laser Raman Spectroscopy"

27.11.84   Dr. W.J. Feast (Durham)
"A Plain Man's Guide to Polymeric Organic Metals"

28.11.84   Dr. T.A. Stephenson (Edinburgh)
"Some Recent Studies in Platinum Metal Chemistry"

12.12.84*   Dr. K.B. Dillon (Durham)
"^{31}P N.M.R. Studies of some Anionic Phosphorus Complexes"

11.1.85*   Emeritus Prof. H. Suschitzky (Salford)
"Fruitful Fissions of Benzofuroxanes and Isobenzimidazoles (umpolung of o-phenylenediamine)"

13.2.85   Dr. G.W.J. Fleet (Oxford)
"Synthesis of some Alkaloids from Carbohydrates"

19.2.85   Dr. D.J. Mincher (Durham)
"Stereoselective Synthesis of some Novel Anthracyclinones Related to the Anti-cancer Drug Adriamycin and to the Steffimycin Antibiotics"

27.2.85*   Dr. R.E. Mulvey (Durham)
"Some Unusual Lithium Complexes"

6.3.85   Dr. P.J. Kocienski (Leeds)
"Some Synthetic Applications of Silicon-Mediated Annulation Reactions"

7.3.85   Dr. P.J. Rodgers (I.C.I. plc, Agricultural Division, Billingham)
"Industrial Polymers from Bacteria"

12.3.85*   Prof. K.J. Packer (B.P. Ltd./East Anglia)
             "N.M.R. Investigations of the Structure of Solid
             Polymers"

14.3.85   Prof. A.R. Katritzky F.R.S. (Florida)
             "Some Adventures in Heterocyclic Chemistry"

20.3.85   Dr. M. Poliakoff (Nottingham)
             "New Methods for Detecting Organometallic
             Intermediates in Solution"

28.3.85   Prof. H. Ringsdorf (Mainz)
             "Polymeric Liposomes as Models for Biomembranes and
             Cells?"

24.4.85   Dr. M.C. Grossel (Bedford College, London)
             "Hydroxypyridone Dyes - Bleachable One-dimensional
             Metals?"

25.4.85   Major S.A. Shackelford (U.S. Air Force)
             "In Situ Mechanistic Studies on Condensed Phase
             Thermochemical Reaction Processes: Deuterium
             Isotope Effects in HMX Decomposition, Explosives
             and Combustion"

1.5.85   Dr. D. Parker (I.C.I. plc, Petrochemical and
             Plastics Division, Wilton)
             "Applications of Radioisotopes in Industrial
             Research"

7.5.85*   Prof. G.E. Coates (formerly of University of
             Wyoming, U.S.A.)
             "Chemical Education in England and America:
             Successes and Deficiencies"

8.5.85   Prof. D. Tuck (Windsor, Ontario)
             "Lower Oxidation State Chemistry of Indium"

3.5.85   Prof. G. Williams (U.C.W. Aberystwyth)
             "Liquid Crystalline Polymers"

9.5.85*   Prof. R.K. Harris (Durham)
             "Chemistry in a Spin: Nuclear Magnetic Resonance"

14.5.85   Prof. J. Passmore (New Brunswick, U.S.A.)
             "The Synthesis and Characterisation of some Novel
             Selenium-Iodine Cations, Aided by ^{77}Se N.M.R.
             Spectroscopy"

15.5.85   Dr. J.E. Packer (Auckland, New Zealand)
             "Studies of Free Radical Reactions in Aqueous
             Solution Using Ionising Radiation"

17.5.85   Prof. I.D. Brown (McMaster University, Canada)
             "Bond Valence as a Model for Inorganic Chemistry"

21.5.85	Dr. D.L.H. Williams (Durham) "Chemistry in Colour"
22.5.85	Dr. M. Hudlicky (Blacksburg, U.S.A.) "Preferential Elimination of Hydrogen Fluoride from Vicinal Bromofluorocompounds"
22.5.85	Dr. R. Grimmett (Otago, New Zealand) Some Aspects of Nucleophilic Substitution in Imidazoles"
4.6.85	Dr. P.S. Belton (Food Research Institute, Norwich) "Analytical Photoacoustic Spectroscopy"
13.6.85	Dr. D. Woolins (Imperial College, London) "Metal - Sulphur - Nitrogen Complexes"
14.6.85*	Prof. Z. Rappoport (Hebrew University, Jerusalem) "The Rich Mechanistic World of Nucleophilic Cinylic Substitution"
19.6.85*	Dr. T.N. Mitchell (Dortmund) "Some Synthetic and NMR - Spectroscopic Studies of Organotin Compounds"
26.6.85	Prof. G. Shaw (Bradford) "Synthetic Studies on Imidazole Nucleosides and the Antibiotic Coformycin"
12.7.85	Dr. K. Laali (Hydrocarbon Research Institute, University of California) "Recent Developments in Superacid Chemistry and Mechanistic Considerations in Electrophilic Aromatic Substitution: A Progress Report"
13.9.85	Dr. V.S. Parmar (University of Delhi) "Enzyme Assisted ERC Synthesis"
30.10.85	Dr. S.N. Whittleton (Durham) "An Investigation of a Reaction Window"
5.11.85	Prof. M.J. O'Donnell (Indiana-Perdue University) "New Methodology for the Synthesis of Amino Acids"
20.11.85	Dr. J.A.H. MacBride (Sunderland Polytechnic) "A Heterocyclic Tour on a Distorted Tricycle-Biphenylene"
28.11.85	Prof. D.J. Waddington (York) "Resources for the Chemistry Teacher"
15.01.86	Prof. N. Sheppard (East Anglia) "Vibrational and Spectroscopic Determinations of the Structures of Molecules Chemisorbed on Metal Surfaces"

29.1.86   Dr. J.H. Clark (York)
             "Novel Fluoride Ion Reagents"

12.2.86   Prof. O.S. Tee (Concordia University, Montreal)
             "Bromination of Phenols"

19.02.86   Prof. G. Procter (Salford)
             "Approaches to the Synthesis of Natural Products"

26.2.86   Miss C. Till (Durham)
             "ESCA and Optical Emission Studies of the Plasma
             Polymerisation of Perfluoroaromatics"

5.3.86   Dr. D. Hathaway (Durham)
             "Herbicide Selectivity"

5.3.86   Dr. M. Schröder (Edinburgh)
             "Studies on Macrocycle Complexes"

12.3.86*   Dr. J.M. Brown (Oxford)
             "Chelate Control in Homogeneous Catalysis"

14.5.86   Dr. P.R.R. Langridge-Smith (Edinburgh)
             "Naked Metal Clusters - Synthesis, Characterisation
             and Chemistry"

9.6.86   Prof. R. Schmutzler (University of Braunschweig)
             "Mixed Valence Diphosphorus Compounds"

23.6.86   Prof. R.E. Wilde (Texas Technical University)
             "Molecular Dynamic Processes from Vibrational
             Bandshapes"

(2) LECTURES ORGANISED BY DURHAM UNIVERSITY CHEMICAL SOCIETY
     DURING THE PERIOD 1983-86

     * Denotes lectures attended.

20.10.83*   Prof. R.B. Cundall (Salford)
             "Explosives"

3.11.83*   Dr. G. Richards (Oxford)
             "Quantum Pharmacology"

10.11.83   Prof. J.H. Ridd (U.C.L.)
             "Ipso-Attack in Electrophilic Aromatic
             Substitution"

17.11.83*   Dr. J. Harrison (Sterling Organics)
             "Applied Chemistry and the Pharmaceutical Industry"
             (Joint Lecture with the Society of Chemical
             Industry)

24.11.83   Prof. D.A. King (Liverpool)
             "Chemistry in 2-Dimensions"

1.12.83   Dr. J.D. Coyle (The Open University)
               "The Problem with Sunshine"

26.1.84   Prof. T.L. Blundell (Birkbeck College, London)
               "Biological Recognition: Interactions of
               Macromolecular Surfaces"

2.2.84   Prof. N.B.H. Jonathan (Southampton)
               "Photoelectron Spectroscopy - A Radical Approach"

16.2.84*   Prof. D. Phillips (The Royal Institution)
               "Luminescence and Photochemistry - A Light
               Entertainment"

23.2.84   Prof. F.G.A. Stone, F.R.S. (Bristol)
               "The Use of Carbene and Carbyne Groups to
               Synthesise Metal Clusters"
               (The Waddington Memorial Lecture)

1.3.84*   Prof. A.J. Leadbetter (Rutherford Appleton Labs.)
               "Liquid Crystals"

8.3.84   Prof. D. Chapman (Royal Free Hospital School of
               Medicine, London)
               "Phospholipids and Biomembranes: Basic Science and
               Future Techniques"

28.3.84   Prof. H. Schmidbaur (Munich, F.R.G.)
               "Ylides in Coordination Sphere of Metal:
               Synthetic, Structural and Theoretical Aspects"
               (R.S.C. Centenary Lecture)

18.10.84*   Dr. N. Logan (Nottingham)
               "N_2O_4 and Rocket Fuels"

23.10.84   Dr. W.J. Feast (Durham)
               "Syntheses of Conjugated Polymers. How and Why?"

8.11.84*   Prof. B.J. Aylett (Queen Mary College, London)
               "Silicon - Dead Common or Refined?"

15.11.84*   Prof. B.T. Golding (Newcastle-upon-Tyne)
               "The Vitamin B_{12} Mystery"

22.11.84*   Prof. D.T. Clark (I.C.I. New Science Group)
               "Structure, Bonding, Reactivity and Synthesis as
               Revealed by ESCA"
               (R.S.C. Tilden Lecture)

29.11.84   Prof. C.J.M. Stirling (University College of North
               Wales)
               "Molecules taking the Strain"

6.12.84*   Prof. R.D. Chambers (Durham)
               "The Unusual World of Fluorine"

24.1.85*   Dr. A.K. Covington (Newcastle-upon-Tyne)
               "Chemistry with Chips"

31.1.85   Dr. M.L.H. Green (Oxford)
               "Naked Atoms and Negligee Ligands"

7.2.85   Prof. A. Ledwith (Pilkington Bros.)
               "Glass as a High Technology Material"
               (Joint Lecture with the Society of Chemical
               Industry)

14.2.85   Dr. J.A. Salthouse (Manchester)
               "Son et Lumiere"

21.2.85*   Prof. P.M. Maitlis, F.R.S. (Sheffield)
               "What Use is Rhodium"

7.3.85*   Dr. P.W. Atkins (Oxford)
               "Magnetic Reactions"

17.10.85*   Dr. C.J. Ludman (Durham)
               "Some Thermochemical Aspects of Explosions"

24.10.85   Dr. J. Dewing (U.M.I.S.T.)
               "Zeolites - Small Holes, Big Opportunities"

31.10.85*   Dr. P. Timms (Bristol)
               "Some Chemistry of Fireworks)

7.11.85   Prof. G. Ertl (University of Munich)
               "Heterogeneous Catalysis"
               (R.S.C. Centenary Lecture)

14.11.85*   Dr. S.G. Davies (Oxford)
               "Chirality Control and Molecular Recognition"

21.11.85   Prof. K.J. Jack, F.R.S. (Newcastle-upon-Tyne)
               "Chemistry of Si-Al-O-N Engineering Ceramics"

28.11.85*   Dr. B.A.J. Clark (Research Division, Kodak Ltd.)
               "Chemistry and Principles of Colour Photography"

23.1.86*   Prof. Sir Jack Lewis, F.R.S. (Cambridge)
               "Some More Recent Aspects in the Cluster Chemistry
               of Ruthenium and Osmium Carbonyls"
               (The Waddington Memorial Lecture)

30.1.86*   Dr. N.J. Phillips (Loughborough)
               "Laser Holography"

13.2.86   Prof. R. Grigg (Queens University, Belfast)
               "Thermal Generation of 1,3-Dipoles"
               (R.S.C. Tilden Lecture)

20.2.86*   Dr. C.F.J. Barnard (Johnson Matthey Group Research)
               "Platinum Anti-Cancer Drug Development - from
               Serendipity to Science"

27.2.86*   Prof. R.K. Harris (Durham)
            "The Magic of Solid State N.M.R."

6.3.86   Dr. B. Iddon (Salford)
            "The Magic of Chemistry"

16.10.86*   Prof. N.N. Greenwood (Leeds)
            "Glorious Gaffes in Chemistry"

(3)   RESEARCH CONFERENCES ATTENDED

       * Indicates Poster Presentation.

19.12.84   18th Sheffield Symposium on "Modern Aspects of
            Stereochemistry", University of Sheffield.

12-17.7.87* Royal Society of Chemistry 3rd International
            Conference on "The Chemistry of the Platinum Group
            Metals", University of Sheffield.

(4)   FIRST YEAR INDUCTION COURSE, OCTOBER 1983

This course consists of a series of one hour lectures on the
services available in the Department.

1.   Departmental organisation

2.   Safety matters

3.   Electrical appliances and infrared spectroscopy

4.   Chromatography and Microanalysis

5.   Atomic absorptiometry and inorganic analysis

6.   Library facilities

7.   Mass spectrometry

8.   Nuclear magnetic resonance spectroscopy

9.   Glassblowing technique.