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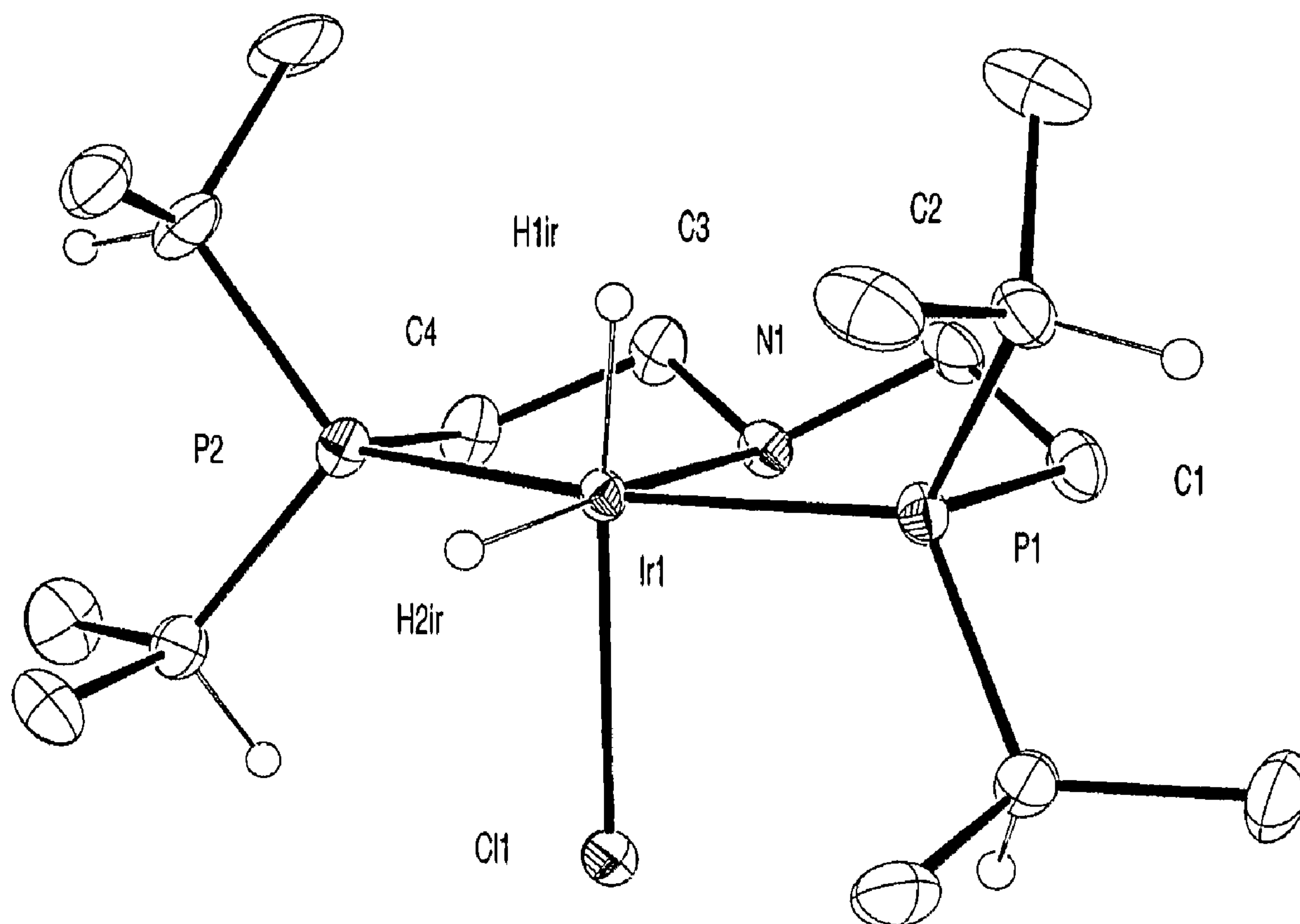
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(54) Title: TRANSFER HYDROGENATION PROCESSES AND CATALYSTS



(57) Abrégé/Abstract:

The invention relates to a process for the reduction of compounds comprising a carbon-carbon (C=C), carbon-oxygen (C=O), or carbon-nitrogen (C=N) double bond, to a corresponding hydrogenated alkane, alcohol or amine, comprising contacting a compound comprising the C=C, C=O or C=N double bond with a hydrogen donor solvent and a catalyst comprising a metal complex having a tridentate aminodiphosphine ligand under transfer hydrogenation conditions.



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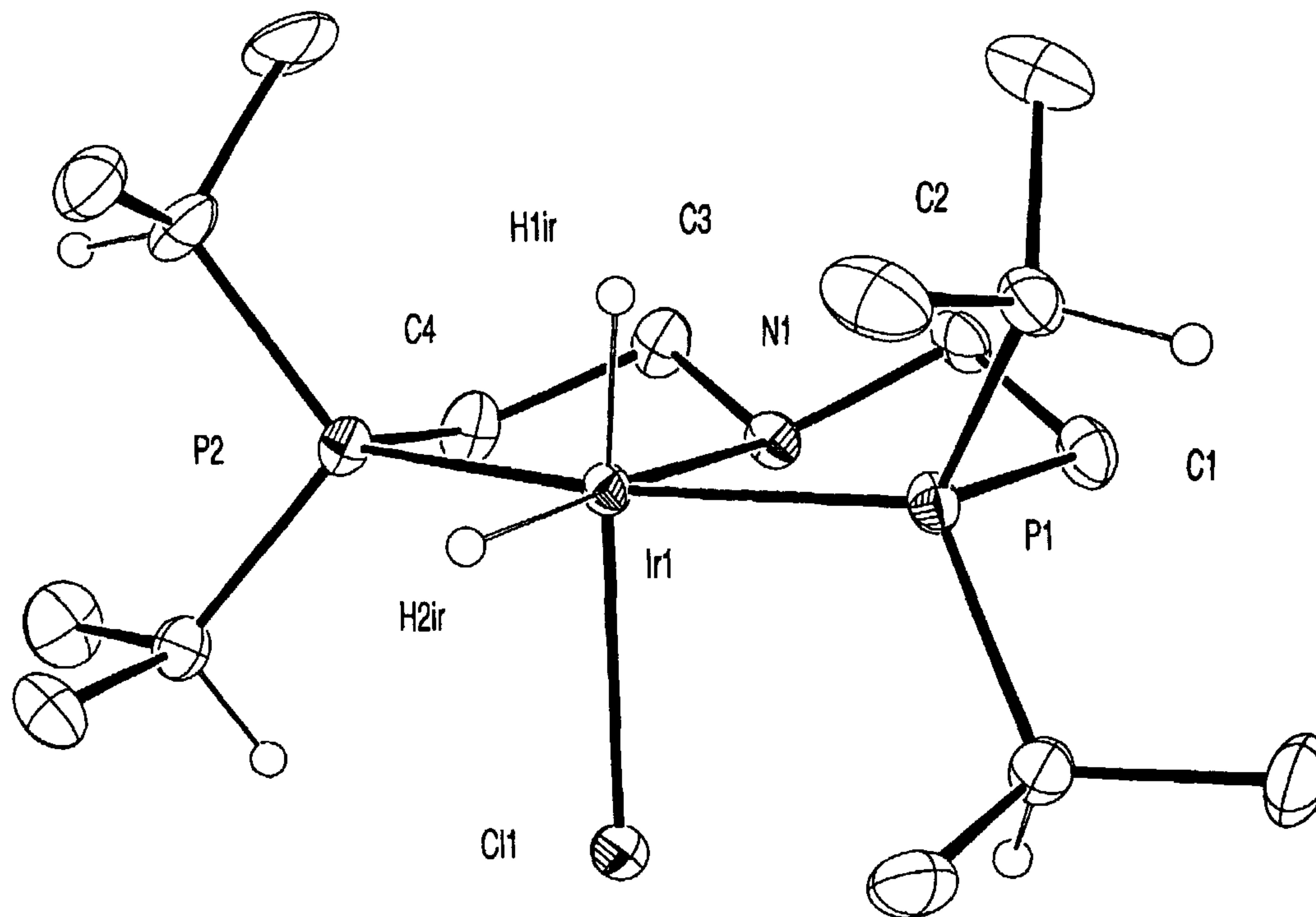
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(57) Abstract: The invention relates to a process for the reduction of compounds comprising a carbon-carbon (C=C), carbon-oxygen (C=O), or carbon-nitrogen (C=N) double bond, to a corresponding hydrogenated alkane, alcohol or amine, comprising contacting a compound comprising the C=C, C=O or C=N double bond with a hydrogen donor solvent and a catalyst comprising a metal complex having a tridentate aminodiphosphine ligand under transfer hydrogenation conditions.

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TITLE: TRANSFER HYDROGENATION PROCESSES AND CATALYSTS
FIELD OF THE INVENTION

The present invention relates to the field of catalytic transfer
5 hydrogenation, in which a catalytic system comprising a metal complex containing a
tridentate aminodiphosphine ligand and a hydrogen donor solvent is used for the
reduction of compounds containing a carbon-carbon (C=C) or a carbon-heteroatom
(C=O, C=N) double bond. In particular, this invention relates to the process of
making optically active compounds.

10 **BACKGROUND OF THE INVENTION**

Catalytic hydrogenation is one of the fundamental reactions in
chemistry, and is used in a large number of chemical processes. It is now recognized
that catalytic hydrogenations of carbon-carbon double bonds of alkenes, and carbon-
heteroatom double bonds of ketones, aldehydes and imines are indispensable
15 processes for the production of the wide range of alkanes, alcohols and amines,
including chiral compounds, which are useful as valuable end products and precursors
for the pharmaceutical, agrochemical, flavor, fragrance, material and fine chemical
industries.

Amongst the several different kinds of processes known to achieve
20 such transformation, two important types are: (a) transfer hydrogenation processes, in
which hydrogen-donors such as secondary alcohols, and in particular isopropanol
(ⁱPrOH), and triethylammonium formate (HCOOH/NEt₃) are used, (b) hydrogenation
processes, in which molecular hydrogen is used. Both hydrogen transfer and
hydrogenation processes need a catalyst or catalytic system to activate the reducing
25 agent, such as an alcohol, HCOOH/NEt₃ or molecular hydrogen.

The catalytic hydrogenation processes developed by Noyori and
coworkers (Ohkuma et al., *J. Am. Chem. Soc.*, 1995, 107, 2675 and 10417) are very
attractive, since the catalysts consist of air-stable ruthenium complexes of the type
RuCl₂(PR₃)₂(diamine) and RuCl₂(diphosphine)(diamine) which are precursors for the
30 generation of what appears to be some of the most active catalysts for the
homogeneous and asymmetric hydrogenation of ketones and imines in the presence of
a base and hydrogen gas. It has been proposed and subsequently mechanistically

elucidated that the key molecular recognition feature of these catalysts is the presence of mutually cis N-H and Ru-H moieties of the catalytic dihydride species ($\text{RuH}_2(\text{PR}_3)_2(\text{diamine})$ and $\text{RuH}_2(\text{diphosphine})(\text{diamine})$) that electronically bind and activate the substrate and facilitate reduction.

5 Transfer hydrogenation, whereby a hydrogen donor solvent such as 2-propanol or $\text{HCOOH}/\text{NEt}_3$ serves as the reducing agent, though currently not as highly developed as catalytic hydrogenation, is widely recognized as a potentially lucrative niche technology that is particularly significant and attractive whenever hydrogenation, for whatever reason, is not applicable or practical. Hence, transfer
10 hydrogenation is complimentary to hydrogenation processes, especially for small to medium scale transformations. In most cases, 2-propanol is the conventional hydrogen donor solvent of choice because it is stable, non-toxic, has a moderate boiling point (82°C), is readily available, inexpensive and environmentally friendly.

 Amongst the potentially interesting transfer hydrogenation catalysts
15 reported in the prior art to activate 2-propanol, there are ruthenium complexes with tetradentate diaminediphosphine ligands, (Gao *et al.* in Tianranqi Huagong, 1995, 20, 1 or CN 1047597 B) and the analogous ruthenium complexes with tetradentate diiminediphosphine ligands, (Xu *et al.* in Yingyong Huaxue 1997, 14, 58 or Gao *et al.* in Chirality, 2000, 12, 383). The reported processes, using these two types of
20 complexes relates to their use for the reduction of carbon-oxygen double bonds, such as those found in ketones and aldehydes.

 Noyori and coworkers have also described an efficient catalyst system generated from the complex $\text{Ru}(\eta^6\text{-arene})(\text{tosyldiamine})\text{Cl}$ for the asymmetric hydrogenation of ketones and imines by transferring hydrogen from
25 triethylammonium formate (Noyori *et al.*, *Acc. Chem. Res.* 1997, 30, 97-102). More recently, Blacker *et al.* demonstrated that cyclopentadienylrhodium and areneruthenium complexes in the presence of tosylated diamines and aminoalcohols are very efficient catalysts for the transfer hydrogenation of a wide range of ketones, imines and iminium salts under mild reaction conditions (A.J. Blacker *et al.*, US
30 6,372,931 B1, 2002; US 6,509,467 B1, 2003).

 There are some reports in the literature of the preparation of tridentate aminodiphosphine ligands and their transition metal complexes, including the use of

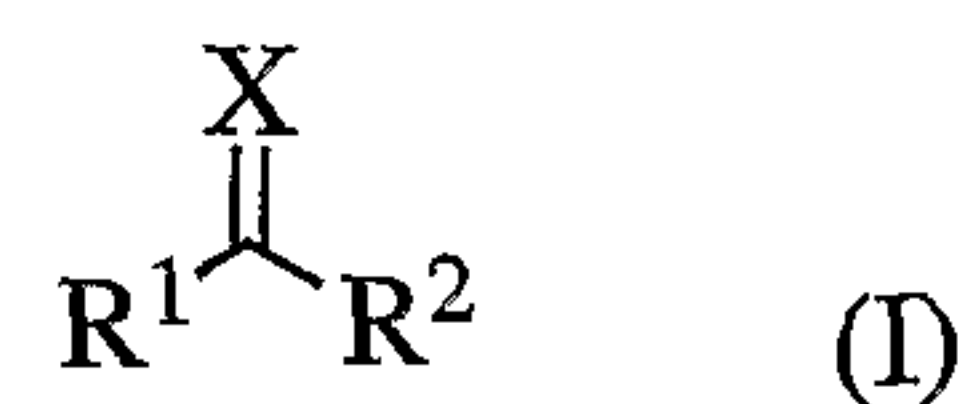
some of these complexes for hydrogenation reactions, involving the use of hydrogen gas as the reducing agent (M.J. Burk et al., *Tetrahedron: Asymmetry*, 1991, 2, 569; M.J. Burk et al., US5,258,553, 1993; M.M. Taqui Khan et al., *J. Mol. Catal.*, 1987, 42, 161; M.M. Taqui Khan et al., *Polyhedron*, 1987, 6, 1727). Surprisingly, none of these reports describes processes in which such complexes are used for transfer hydrogenation processes, involving a hydrogen donor solvent as the reducing agent.

SUMMARY OF THE INVENTION

It has now been found that metal complexes comprising tridentate aminodiphosphine ligands are particularly efficient catalysts for the reduction of carbon-carbon and carbon-heteroatom double bonds under transfer hydrogenation conditions.

Therefore, the present invention includes a process for the reduction of compounds comprising a carbon-carbon (C=C), carbon-oxygen (C=O) or carbon-nitrogen (C=N) double bond, to a corresponding hydrogenated alkane, alcohol or amine, comprising contacting a compound comprising the C=C, C=O or C=N double bond with a hydrogen donor and a catalyst comprising a metal complex having a tridentate aminodiphosphine ligand under transfer hydrogenation conditions.

In an embodiment of the invention, the compound comprising a carbon-carbon (C=C), carbon-oxygen (C=O) or carbon-nitrogen (C=N) double bond is a compound of formula (I):



wherein,

X is selected from the group consisting of CR³R⁴, NR⁵, (NR⁵R⁶)⁺Q⁻ and O;

R¹ and R² each simultaneously or independently are selected from the group consisting of H, aryl, C₁₋₂₀alkyl, C₂₋₂₀alkenyl, C₃₋₂₀cycloalkyl and heteroaryl, said latter 5 groups being optionally substituted, or R¹ and R² are linked to form an optionally substituted ring;

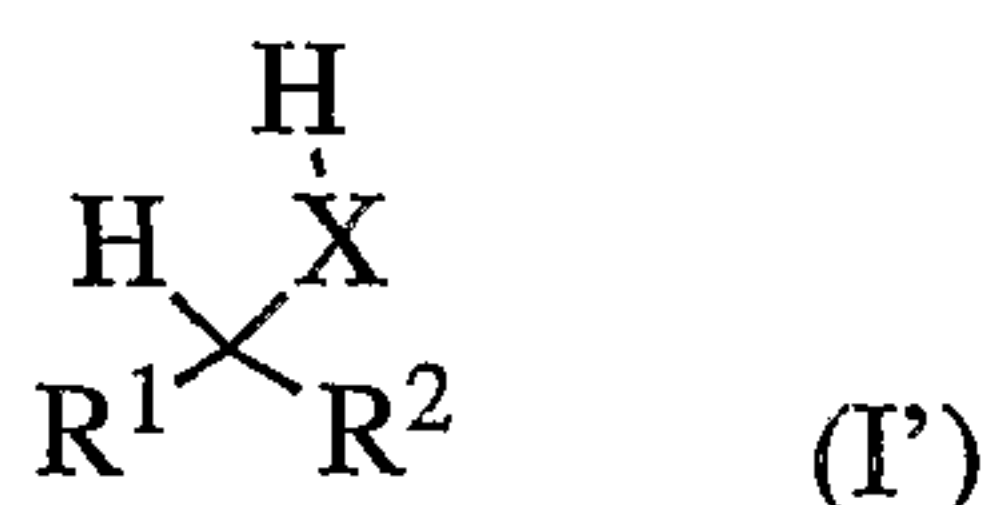
R³ to R⁶ each independently or simultaneously are selected from the group consisting of H, OH, C₁₋₂₀alkoxy, aryloxy, C₁₋₂₀alkyl, C₂₋₂₀alkenyl, C₃₋₂₀cycloalkyl and aryl, said

latter 6 groups being optionally substituted, or one or more of R^1 to R^6 are linked to form an optionally substituted ring or rings; and

Q^- represents an anion,

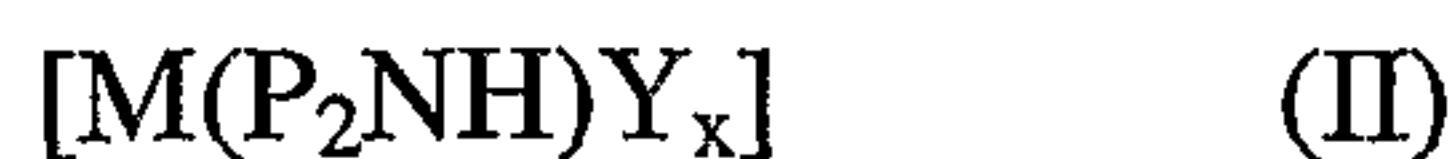
wherein heteroaryl is a mono- or bicyclic heteroaromatic radical containing from 5 to 10 atoms, of which 1-3 atoms may be a heteroatom selected from the group consisting of S, O and N, and wherein the optional substituents are selected from the group consisting of halo, OH, NH_2 , OR^c , NR^c_2 or R^c groups, in which R^c is selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl and aryl and. one or more of the carbon atoms in the alkyl, alkenyl and cycloalkyl groups may be optionally substituted with a heteroatom selected from the group consisting of O, S, N, P and Si.

Reduction of compounds of formula I using the process of the invention provides the corresponding hydrogenated compounds of formula (I'):



wherein X, R^1 and R^2 are defined as in formula (I).

The processes of the invention are characterized by the use of a catalytic system comprising a metal complex with a tridentate aminodiphosphine ligand with or without a base. Useful complexes are of the general formula



wherein

M is a metal;

Y simultaneously or independently are any anionic or neutral ligand, and the ligand (P_2NH) represents a tridentate aminodiphosphine ligand of formula (III):

$$\begin{array}{c}
 \text{R}^9 \\
 | \\
 \text{---} \text{---} \text{---} \text{PR}_2 \\
 | \\
 \text{R}^8 \\
 | \\
 \text{NH} \\
 | \\
 \text{R}^7 \\
 | \\
 \text{---} \text{---} \text{---} \text{PR}_2 \\
 | \\
 \text{R}^{10}
 \end{array}
 \quad (\text{III})$$

Figure 1 shows an x-ray structure of the complex $\text{IrH}_2\text{Cl}[(^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH}]$.

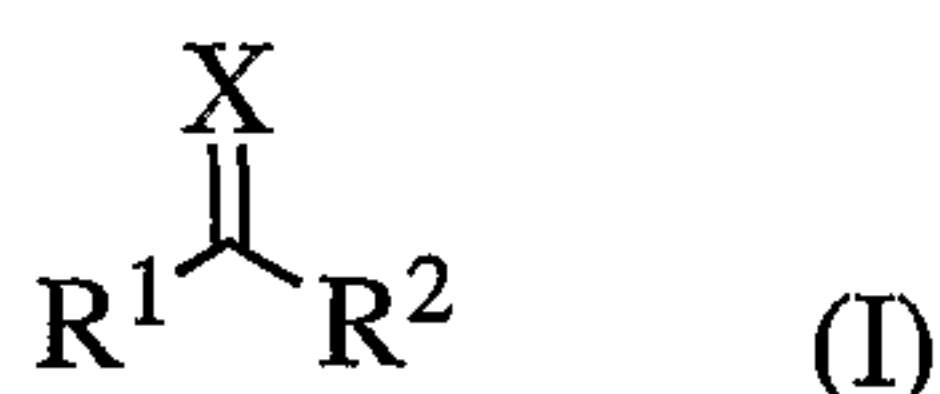
DETAILED DESCRIPTION OF THE INVENTION

It has found that tridentate aminodiphosphine ligands, when complexed with a metal, are particularly efficient catalysts for the reduction of C=C, C=O and C=N double bonds under transfer hydrogenation conditions.

5 Accordingly, the present invention relates to a process for the reduction of compounds comprising a carbon-carbon (C=C), carbon-oxygen (C=O) or carbon-nitrogen (C=N) double bond, to a corresponding hydrogenated alkane, alcohol or amine, comprising contacting a compound comprising the C=C, C=O or C=N double bond with a hydrogen donor and a catalyst comprising a metal complex having
10 a tridentate aminodiphosphine ligand under transfer hydrogenation conditions.

The compound comprising a C=C, C=O or C=N, includes compounds having one or more C=C, C=O and/or C=N bonds.

In an embodiment of the invention, the compound comprising a carbon-carbon (C=C), carbon-oxygen (C=O) or carbon-nitrogen (C=N) double bond
15 is a compound of formula (I):

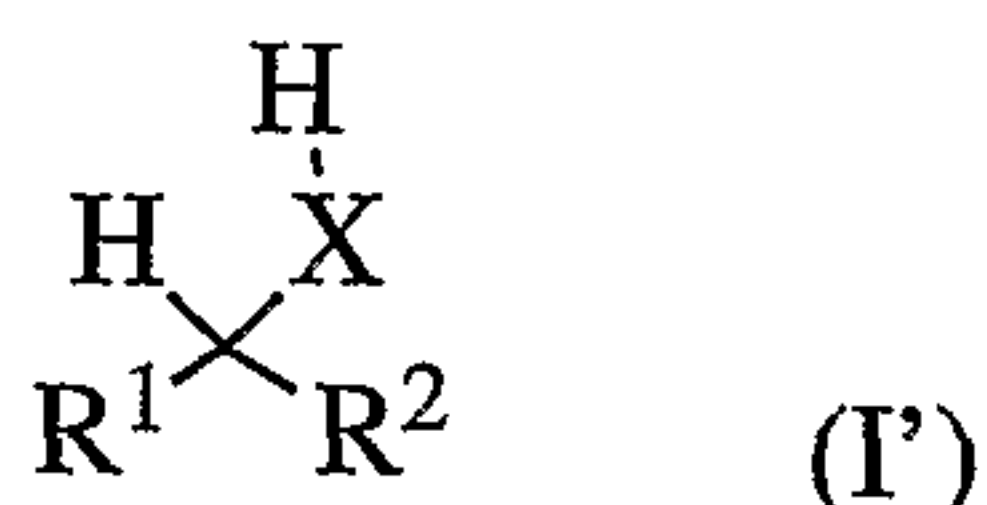


wherein,

- 20 X is selected from the group consisting of CR^3R^4 , NR^5 , $(\text{NR}^5\text{R}^6)^+\text{Q}^-$ and O;
 R^1 and R^2 each simultaneously or independently are selected from the group consisting of H, aryl, C_{1-20} alkyl, C_{2-20} alkenyl, C_{3-20} cycloalkyl and heteroaryl, said latter 5 groups being optionally substituted, or R^1 and R^2 are linked to form an optionally substituted ring;
- 25 R^3 to R^6 each independently or simultaneously are selected from the group consisting of H, OH, C_{1-20} alkoxy, aryloxy, C_{1-20} alkyl, C_{2-20} alkenyl, C_{3-20} cycloalkyl and aryl, said latter 6 groups being optionally substituted, or one or more of R^1 to R^6 are linked to form an optionally substituted ring or rings; and
 Q^- represents an anion,
- 30 wherein heteroaryl is a mono- or bicyclic heteroaromatic radical containing from 5 to 10 atoms, of which 1-3 atoms may be a heteroatom selected from the group consisting

of S, O and N, and wherein the optional substituents are selected from the group consisting of halo, OH, NH₂, OR^c, NR^c₂ or R^c groups, in which R^c is selected from the group consisting of C₁₋₆alkyl, C₂₋₆alkenyl and aryl and. one or more of the carbon atoms in the alkyl, alkenyl and cycloalkyl groups may be optionally substituted with a
 5 heteroatom selected from the group consisting of O, S, N, P and Si.

Reduction of compounds of formula I using the process of the invention provides the corresponding hydrogenated compounds of formula (I'):



10

wherein X, R¹ and R² are defined as in formula (I).

Since R¹ and R² may be different, it is hereby understood that the final product, of formula (I'), may be chiral, thus possibly consisting of a practically pure enantiomer or of a mixture of stereoisomers, depending on the nature of the catalyst
 15 used in the process.

The term "C_{1-n}alkyl" as used herein means straight and/or branched chain alkyl radicals containing from one to "n" carbon atoms and includes methyl, ethyl, propyl, isopropyl, t-butyl, n-decyl and the like.

The term "C_{1-n}alkoxy" as used herein means straight and/or branched
 20 chain alkoxy radicals containing from one to "n" carbon atoms and includes methoxy, ethoxy, propyloxy, isopropoxy, t-butoxy, heptoxy and the like.

The term "aryl" as used herein means unsubstituted or substituted mono- or bicyclic aromatic radicals containing from 6 to 14 carbon atoms and includes phenyl and naphthyl and the like.

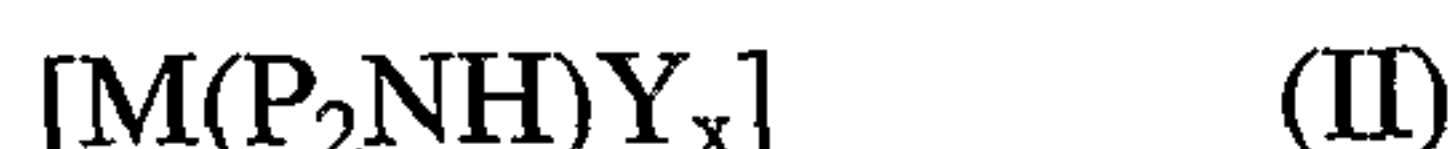
25 The term "heteroaryl" as used herein means unsubstituted or substituted mono- or bicyclic heteroaromatic radicals containing from 5 to 14 atoms, of which 1-3 atoms may be a heteroatom selected from the group consisting of S, O and N, and includes furanyl, thienyl, pyrrolo, pyridyl, indolo, benzofuranyl and the like.

The term "halo" as used herein means halogen and includes chloro, fluoro, bromo, iodo and the like.

The term "C_{2-n}alkenyl" as used herein means straight and/or branched chain alkenyl groups containing from two to "n" carbon atoms and at least one double bond and includes allyl, isoprenyl and the like.

The term "C₃₋₂₀cycloalkyl" as used herein means a saturated carbocyclic group containing from three to twenty carbon atoms and includes cyclopropyl, cyclobutyl, cyclopentyl, cyclodecyl and the like.

The processes of the invention are characterized by the use of a catalytic system comprising a metal complex with a tridentate aminodiphosphine ligand with or without a base. Useful complexes are of the general formula

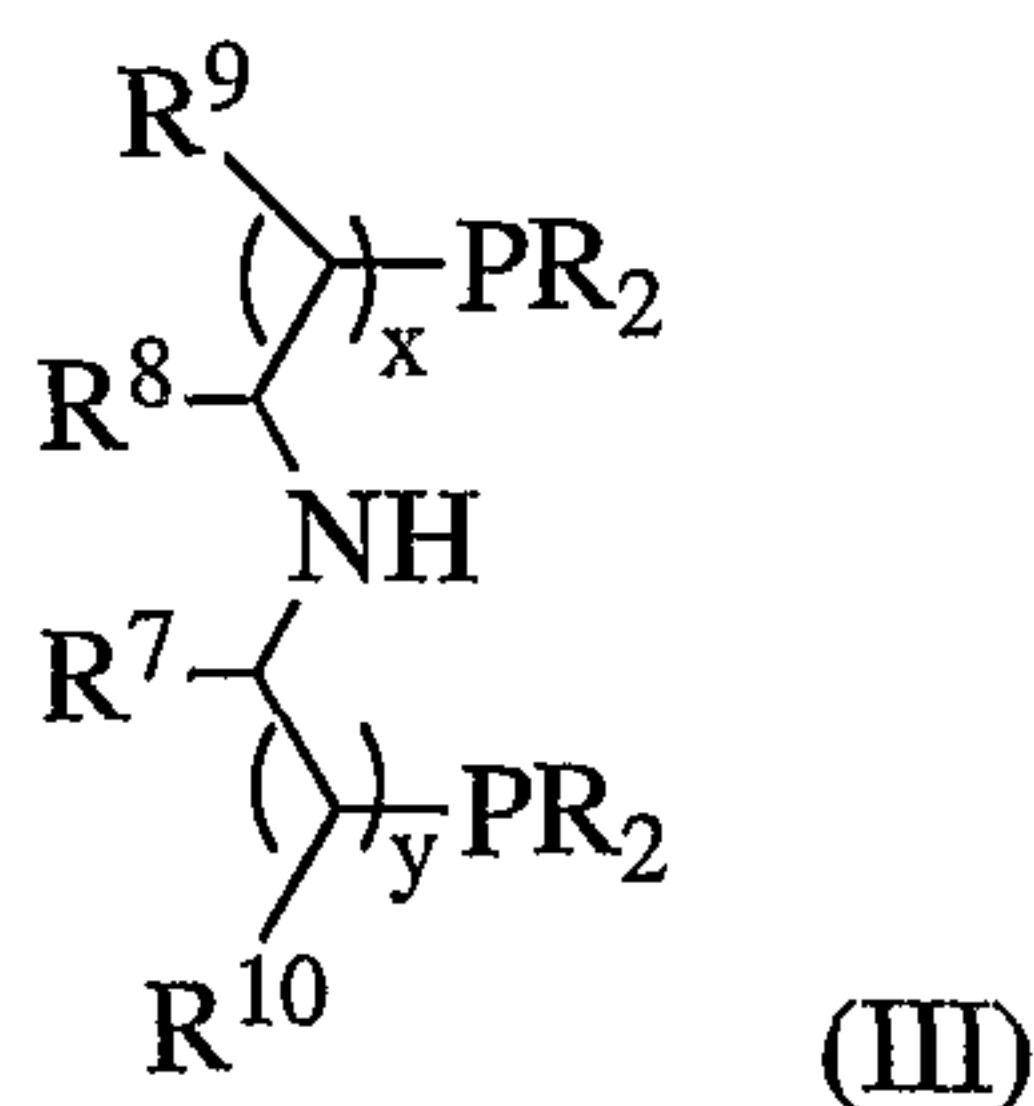


wherein

M is a metal;

Y simultaneously or independently are any anionic or neutral ligand, and

the ligand (P₂NH) represents a tridentate aminodiphosphine ligand of formula (III):



20

in which R⁷ to R¹⁰ simultaneously or independently are selected from the group consisting of H, C₁₋₂₀alkyl, C₂₋₂₀alkenyl, C₃₋₂₀cycloalkyl and aryl, said latter 4 groups being optionally substituted, or two adjacent or geminal groups are bonded together to form an optionally substituted ring;

x and y are, simultaneously or independently, equal to 0, 1, 2, 3 or 4; and

R is simultaneously or independently selected from the group consisting of H, C₁₋₂₀alkyl, aryl and C₂₋₂₀alkenyl, OR and NR₂, said latter 5 groups being optionally

substituted, or the R groups on the same P atom may be bonded together to form an optionally substituted monocyclic or polycyclic, saturated or aromatic ring system having 4 or more atoms, including the phosphorous atom to which said R groups are bonded, and in which one or more carbon atoms in said monocyclic or polycyclic ring system may optionally be replaced with a heteroatom selected from O, S, N, and Si, wherein the optional substituents are selected from one or more of halo, OH, NH₂, OR^c, NR^c₂ and R^c, in which R^c is selected from the group consisting of C₁₋₆alkyl, C₂₋₆alkenyl and aryl.

In the present invention, the tridentate ligand of formula III includes those in which R⁷ to R¹⁰ simultaneously or independently are selected from the group consisting of H, C₁₋₂₀alkyl, C₂₋₂₀alkenyl, C₃₋₂₀cycloalkyl and aryl, said latter 4 groups being optionally substituted, or two adjacent or geminal groups are bonded together to form an optionally substituted ring. In an embodiment of the invention R⁷ to R¹⁰ simultaneously or independently are selected from the group consisting of H, C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₃₋₁₀cycloalkyl and aryl, said latter 4 groups being optionally substituted, or two adjacent or geminal groups are bonded together to form an optionally substituted ring. In further embodiments of the invention, R⁷ to R¹⁰ simultaneously or independently are selected from the group consisting of H, C₁₋₄alkyl, C₂₋₄alkenyl, C₃₋₁₆cycloalkyl and aryl, said latter 4 groups being optionally substituted, or two adjacent or geminal groups are bonded together to form an optionally substituted ring, said ring containing 6 atoms, including the carbons to which said groups are attached. In further embodiments of the invention R⁷ to R¹⁰ are all H.

In the present invention, the tridentate ligand of formula III further includes those in which x and y are, simultaneously or independently, equal to 0, 1, 2, 3 or 4. In embodiments of the invention, x and y are simultaneously equal to 0, 1, 2, 3 or 4. In further embodiments of the invention, x and y are simultaneously equal to 0, 1 or 2. In still further embodiments of the invention, x and y are simultaneously equal to 1.

In the present invention, the tridentate ligand of formula III still further includes those in which R is simultaneously or independently selected from the group consisting of H, C₁₋₂₀alkyl, aryl and C₂₋₂₀alkenyl, OR and NR₂, said latter 5 groups

being optionally substituted, or the R groups on the same P atom may be bonded together to form an optionally substituted monocyclic or polycyclic, saturated or aromatic ring system having 4 or more atoms, including the phosphorous atom to which said R groups are bonded, and in which one or more carbon atoms in said
5 monocyclic or polycyclic ring system may optionally be replaced with a heteroatom selected from O, S, N, and Si. In an embodiment of the invention, R is simultaneously or independently selected from the group consisting of H, C₁₋₁₀alkyl, aryl and C₂₋₁₀alkenyl, said latter 3 groups being optionally substituted, or the R groups on the same P atom may be bonded together to form an optionally substituted
10 monocyclic or polycyclic, saturated or aromatic ring system having 4 or more atoms, including the phosphorous atom to which said R groups are bonded, and in which one or more carbon atoms in said monocyclic or polycyclic ring system may optionally be replaced with a heteroatom selected from O and NH. In still further embodiments of the invention, R is simultaneously or independently selected from the group
15 consisting of H, C₁₋₆alkyl, phenyl, naphthyl and C₂₋₆alkenyl, said latter 3 groups being optionally substituted, or the R groups on the same P atom may be bonded together to form an optionally substituted monocyclic, fused bicyclic, fused tricyclic, fused quadracyclic or fused pentacyclic, saturated or aromatic ring system having 4-23 atoms, including the phosphorous atom to which said R groups are bonded, and in
20 which one or more carbon atoms in said monocyclic or polycyclic ring system may optionally be replaced with a heteroatom selected from O and NH. In a further embodiment of the invention, R is simultaneously C₁₋₆alkyl or phenyl, in particular, methyl, ethyl, propyl, isopropyl, t-butyl, sec-butyl or phenyl.

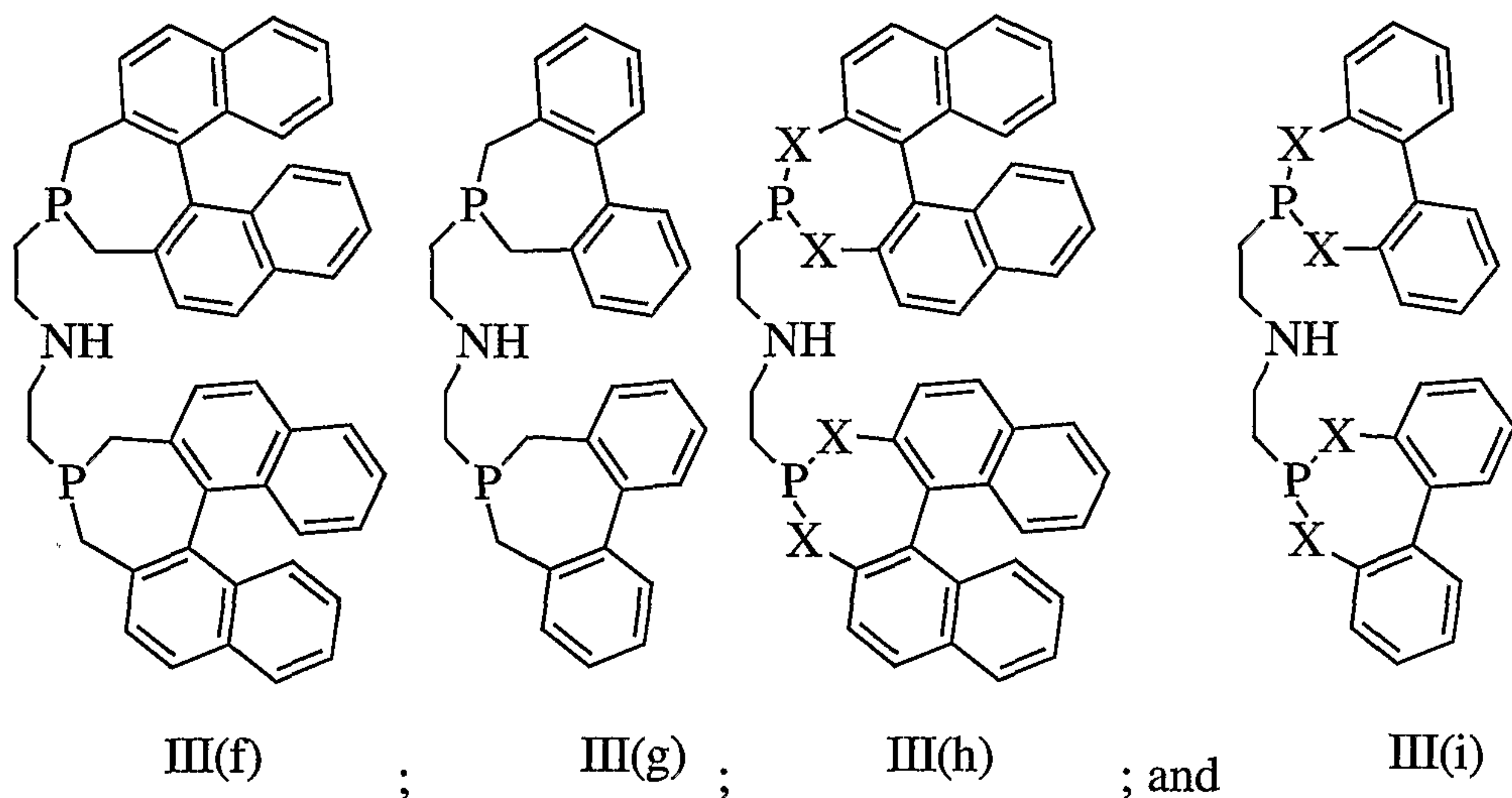
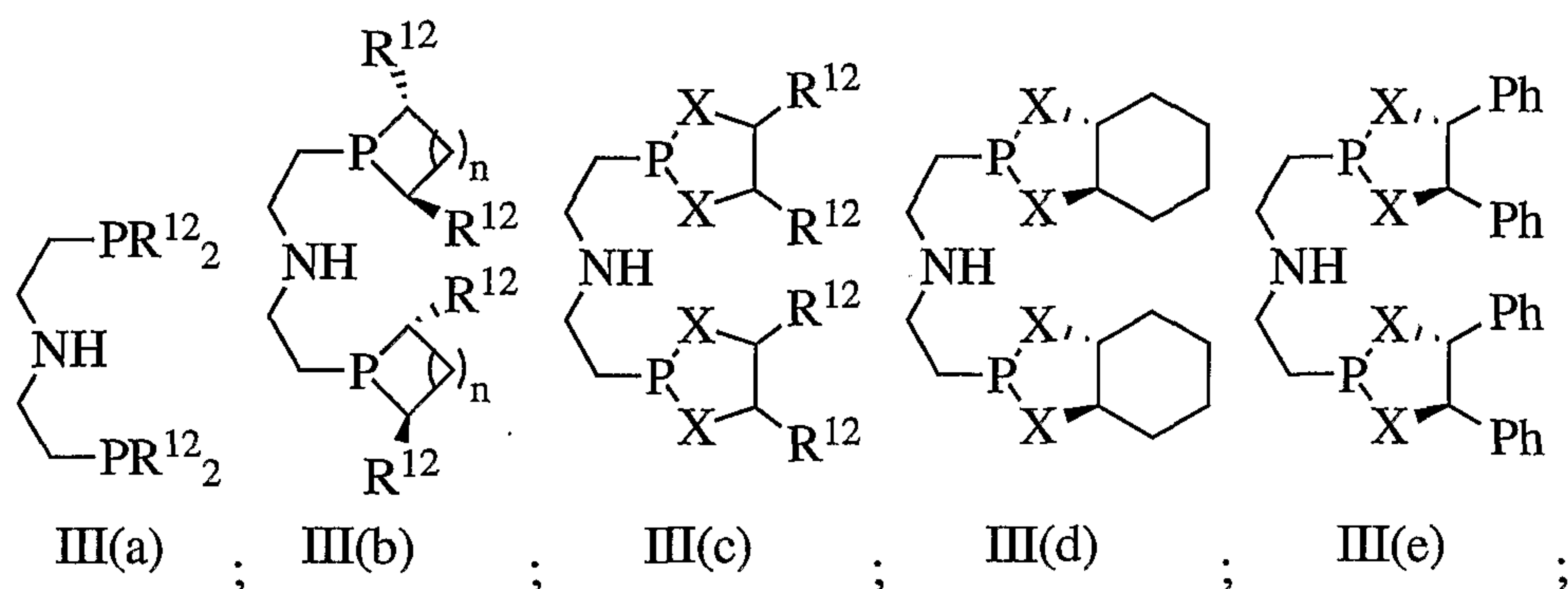
According to the invention, the optional substituents on the
25 compounds of formula III are selected from one or more of halo, OH, NH₂, OR^c, NR^c₂ and R^c, in which R^c is selected from the group consisting of C₁₋₆alkyl, C₂₋₆alkenyl and aryl. In embodiments of the invention, the optional substituents are selected from one or more of halo, OH, NH₂, OR^c, NR^c₂ and R^c, in which R^c is selected from the group consisting of C₁₋₄alkyl, C₂₋₄alkenyl and phenyl. In further embodiments of the
30 invention, the groups R⁷-R¹⁰ and R in the ligands of Formula III are unsubstituted.

The processes of the invention are particularly attractive when the aminodiphosphine ligand (P₂NH) of formula (III) is chiral. Whenever (P₂NH) is

chiral, the process of the invention can be useful in asymmetric transfer hydrogenation.

In embodiments of the present invention, the ligand (P_2NH) is selected from one of the formulae III(a)-III(i) below:

5



10

wherein R^{12} is selected from the group consisting of halo, OH, NH_2 , OR^c , NR^c_2 and R^c in which R^c is selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl and aryl; n is 1 to 6; and X is O, NH or NR^c .

In embodiments of the invention, the ligand P_2NH is a compound of
15 formula III(a) and R^{12} is R^c , in which R^c is selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl and phenyl. In further embodiments of the invention P_2NH is a

compound of formula III(a) and R^{12} is R^c , in which R^c is selected from the group consisting of C_{1-4} alkyl and phenyl, in particular i-propyl and phenyl.

In the catalysts of formula II, the metal, M, is any transition metal of groups 3 through 12 of the periodic table, suitably groups 4 through 10, plus the
5 lanthanides and actinides. Examples of suitable metals include, but are not limited to Co, Rh, Ir, Ru, Os and Re. In an embodiment of the invention, the M is Ir.

The ligand Y, may be a halide; alkyl; aryl; unsaturated hydrocarbyl including but not limited to olefin, diolefin such as cyclooctadiene or norbornadiene or alkyne; acetate; alkoxide; amide; hydride; sulfide; phosphine; carbon monoxide;
10 amine; ether; hydroxide; oxo; imido; or acetylacetonate groups. When the complex has a negative charge, a countercation is required. Examples include ammonium, tetraalkylammonium, sodium, potassium or lithium. When the complex has a positive charge, a counteranion is required. Suitable examples of counteranions are tetrafluoroborate, hexafluoroantimonate or chloride.

15 In a general way, the complexes of formula (II) can be prepared and isolated prior to their use in the process according to the general methods described in the literature or using the methods described herein. Moreover, the complexes can be prepared *in situ*, by several methods, in the reaction medium, without isolation or purification, just before their use.

20 The catalytic system characterizing the process of the instant invention may comprise a base. Said base can be the substrate itself, if the latter is basic, or any conventional base. One can cite, as non-limiting examples, organic non-coordinating bases such as DBU, an alkaline or alkaline-earth metal carbonate, a carboxylate salt such as sodium or potassium acetate, or an alcoholate or hydroxide salt. In an
25 embodiment of the invention, the bases are the alcoholate or hydroxide salts selected from the group consisting of the compounds of formula $(R^{13}O)_2M'$ and $R^{13}OM''$, wherein M' is an alkaline-earth metal, M'' is an alkaline metal and R^{13} stands for hydrogen or a linear or branched alkyl group.

Standard transfer hydrogenation conditions, as used herein, typically
30 implies the mixture of the substrate with a metal complex of formula (II) with or without a base, possibly in the presence of a solvent, and then treating such a mixture with a hydrogen donor solvent at a chosen pressure and temperature.

The complexes of formula (II) can be added to the reaction medium in a large range of concentrations. As non-limiting examples, one can cite as complex concentration values those ranging from 0.1 ppm to 50,000 ppm, relative to the amount of substrate, thus representing respectively a substrate/complex (S/com) ratio of 10^7 to 20. In an embodiment of the invention, the complex concentration will be comprised between 0.1 and 1000 ppm, i.e. a S/com ratio of 10^7 to 1000 respectively. In a further embodiment of the invention, there will be used concentrations in the range of 0.5 to 100 ppm, corresponding to a S/com ratio of 10,000 to 2×10^6 respectively.

If required, useful quantities of base, added to the reaction mixture, may be comprised in a relatively large range. One can cite, as non-limiting examples, ranges between 1 to 50,000 molar equivalents relative to the complex (e.g. base/com = 0.5 to 50,000), or 100 to 20,000, or even between 400 and 10,000 molar equivalents. However, it should be noted that it is also possible to add a small amount of base (e.g. base/com = 1 to 3) to achieve high yields.

In the processes of this invention, the transfer hydrogenation reaction can be carried out in the presence or absence of a solvent. When a solvent is required or used for practical reasons, then any solvent current in transfer hydrogenation reactions can be used for the purposes of the invention. Non-limiting examples include aromatic solvents such as benzene, toluene or xylene, hydrocarbon solvents such as hexane or cyclohexane, ethers such as tetrahydrofuran, or yet primary or secondary alcohols, or mixtures thereof. In another embodiment, the solvent is a primary, secondary or tertiary amine. A person skilled in the art is well able to select the solvent most convenient in each case to optimize the transfer hydrogenation reaction.

Hydrogen donors include primary and secondary alcohols, primary and secondary amines, carboxylic acids and their esters and amine salts, readily dehydrogenatable hydrocarbons, clean reducing agents, and any combination thereof.

Primary and secondary alcohols which may be employed as hydrogen donors comprise commonly from 1 to 10 carbon atoms, specifically from 2 to 7 carbon atoms, and more specifically 3 or 4 carbon atoms. Examples of primary and secondary alcohols that may be represented as hydrogen donors include methanol, ethanol, propan-1-ol, propan-2-ol, butan-1-ol, butan-2-ol, cyclopentanol,

cyclohexanol, benzylalcohol, and menthol. When the hydrogen donor is an alcohol, it is an embodiment of the invention that the alcohol is a secondary alcohols, for example propan-2-ol, and butan-2-ol.

Primary and secondary amines which may be employed as hydrogen
5 donors comprise commonly from 1 to 20 carbon atoms, specifically from 2 to 14 carbon atoms, and more specifically 3 or 8 carbon atoms. Examples of primary and secondary amines, which may be represented as hydrogen donors, include ethylamine, propylamine, isopropylamine, butylamine, isobutylamine, hexylamine, diethylamine, dipropylamine, di-isopropylamine, dibutylamine, di-isobutylamine, dihexylamine,
10 benzylamine, dibenzylamine and piperidine. When the hydrogen donor is an amine, it is an embodiment of the invention that the amine is a primary amines, for example primary amines comprising a secondary alkyl group, such as isopropylamine and isobutylamine.

Carboxylic acids or their esters, which may be employed as hydrogen
15 donors, comprise commonly from 1 to 10 carbon atoms, specifically from 1 to 3 carbon atoms. In certain embodiments, the carboxylic acid is advantageously a beta-hydroxy-carboxylic acid. Esters may be derived from the carboxylic acid and a C₁₋₁₀ alcohol. Examples of carboxylic acids, which may be employed as hydrogen donors include formic acid, lactic acid, ascorbic acid and mandelic acid. When a carboxylic
20 acid is employed as hydrogen donor, it is an embodiment that at least some of the carboxylic acid is present as an amine salt or ammonium salt. Amines, which may be used to form such salts, include both aromatic and non-aromatic amines, also primary, secondary and tertiary amines and comprise typically from 1 to 20 carbon atoms. In an embodiment of the invention the amine is a tertiary amine, for example
25 trialkylamines. Examples of amines, which may be used to form salts, include trimethylamine, triethylamine, di-isopropylethylamine and pyridine. In a further embodiment of the invention, the amine is triethylamine. When at least some of the carboxylic acid is present as an amine salt, particularly when a mixture of formic acid and triethylamine is employed, the mole ratio of acid to amine is commonly about
30 5:2. This ratio may be maintained during the course of the reaction by the addition of either component, but usually by the addition of the carboxylic acid.

Readily dehydrogenatable hydrocarbons, which may be employed as hydrogen donors, comprise hydrocarbons, which have a propensity to aromatise or hydrocarbons, which have a propensity to form highly conjugated systems. Examples of readily dehydrogenatable hydrocarbons, which may be employed as hydrogen donors, include cyclohexadiene, cyclohexane, tetralin, dihydrofuran and terpenes.

Clean reducing agents which may be represented as hydrogen donors comprise reducing agents with a high reduction potential, particularly those having a reduction potential relative to the standard hydrogen electrode far greater than about -0.1 eV, often greater than about -0.5 eV, and preferably greater than about -1 eV. Examples of clean reducing agents, which may be represented as hydrogen donors include hydrazine and hydroxylamine.

In an embodiment of the invention the hydrogen donors are propan-2-ol, butan-2-ol, triethylammonium formate and a mixture of triethylammonium formate and formic acid.

In an embodiment, the transfer hydrogenation procedure is carried out in the presence of an inert gas or in the presence of air.

The temperature at which the transfer hydrogenation can be carried out is comprised between 0°C and 100°C , more specifically in the range of between 20°C and 80°C . Of course, a person skilled in the art is also able to select the temperature as a function of the melting and boiling point of the starting and final products.

The following non-limiting examples are illustrative of the present invention:

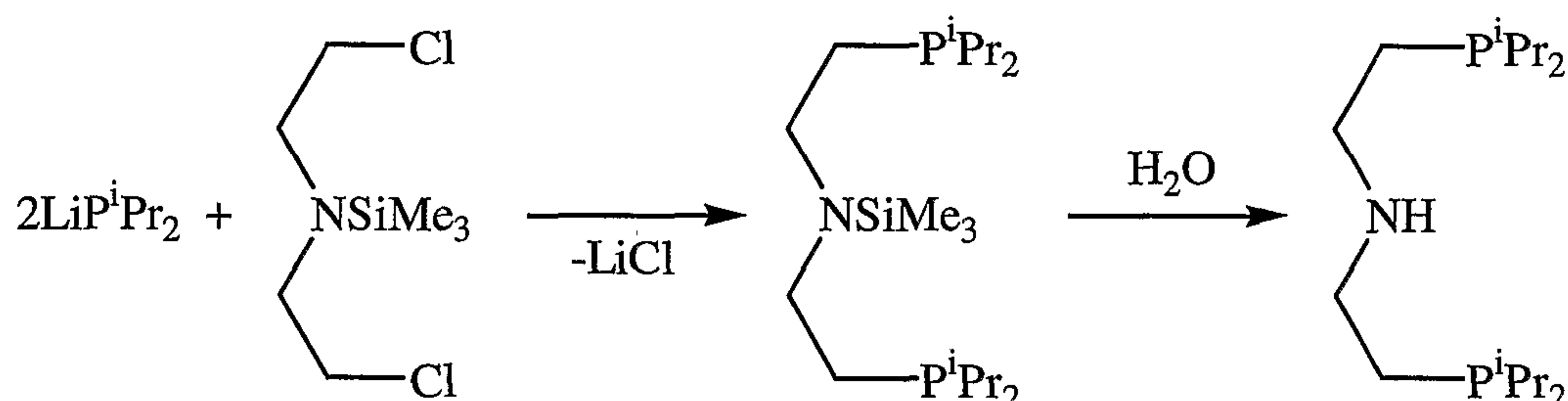
20 EXAMPLES

The invention will now be described in further details by way of the following examples, wherein the temperatures are indicated in degrees centigrade and the abbreviations have the usual meaning in the art. All the procedures described hereafter have been carried out under an inert atmosphere unless stated otherwise. All preparations and manipulations were carried out under H_2 , N_2 or Ar atmospheres with the use of standard Schlenk, vacuum line and glove box techniques in dry, oxygen-free solvents. Tetrahydrofuran (THF), diethyl ether (Et_2O) and hexanes were dried and distilled from sodium benzophenone ketyl. Deuterated solvents were degassed and dried over activated molecular sieves. Ruthenium trichloride, iridium trichloride, chlorodiisopropylphosphine, chlorodiphenylphosphine, ketones and amines were purchased from Aldrich. NMR spectra were recorded on a 300 MHz spectrometer

(300 MHz for ^1H , 75 MHz for ^{13}C and 121.5 for ^{31}P). All ^{31}P chemical shifts were measured relative to 85% H_3PO_4 as an external reference. ^1H and ^{13}C chemical shifts were measured relative to partially deuterated solvent peaks but are reported relative to tetramethylsilane.

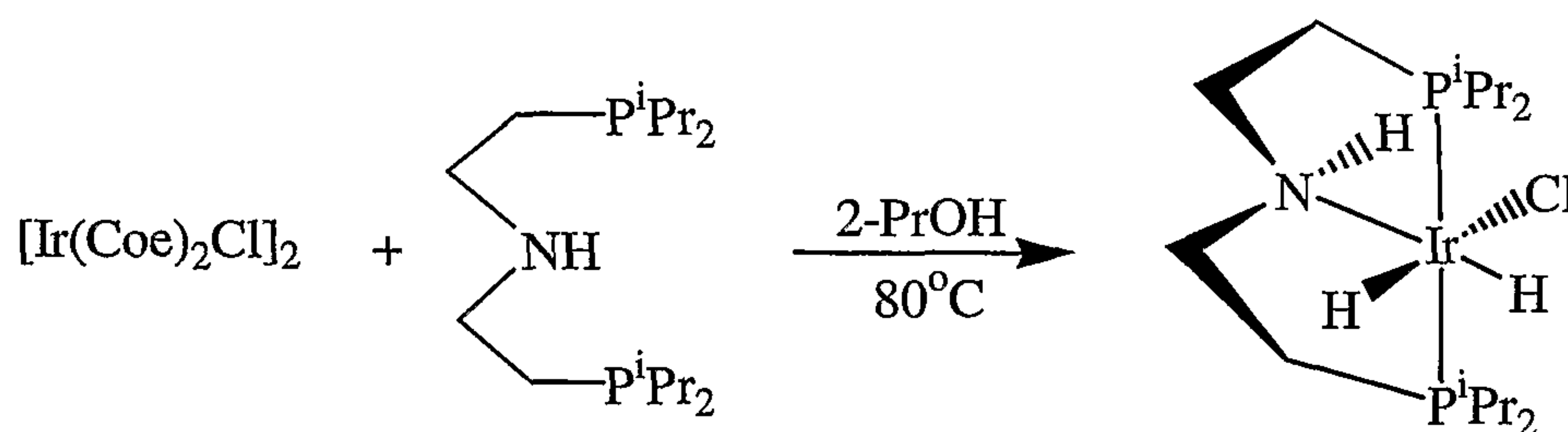
5 **Example 1 : Preparation of the Ligand Bis(2-(diisopropylphosphino)ethyl)amine, ($^i\text{Pr}_2\text{PC}_2\text{H}_4$) $_2\text{NH}$ and Iridium complexes**

Example 1.1 Preparation of Bis(2-(diisopropylphosphino)ethyl)amine, ($^i\text{Pr}_2\text{PC}_2\text{H}_4$) $_2\text{NH}$



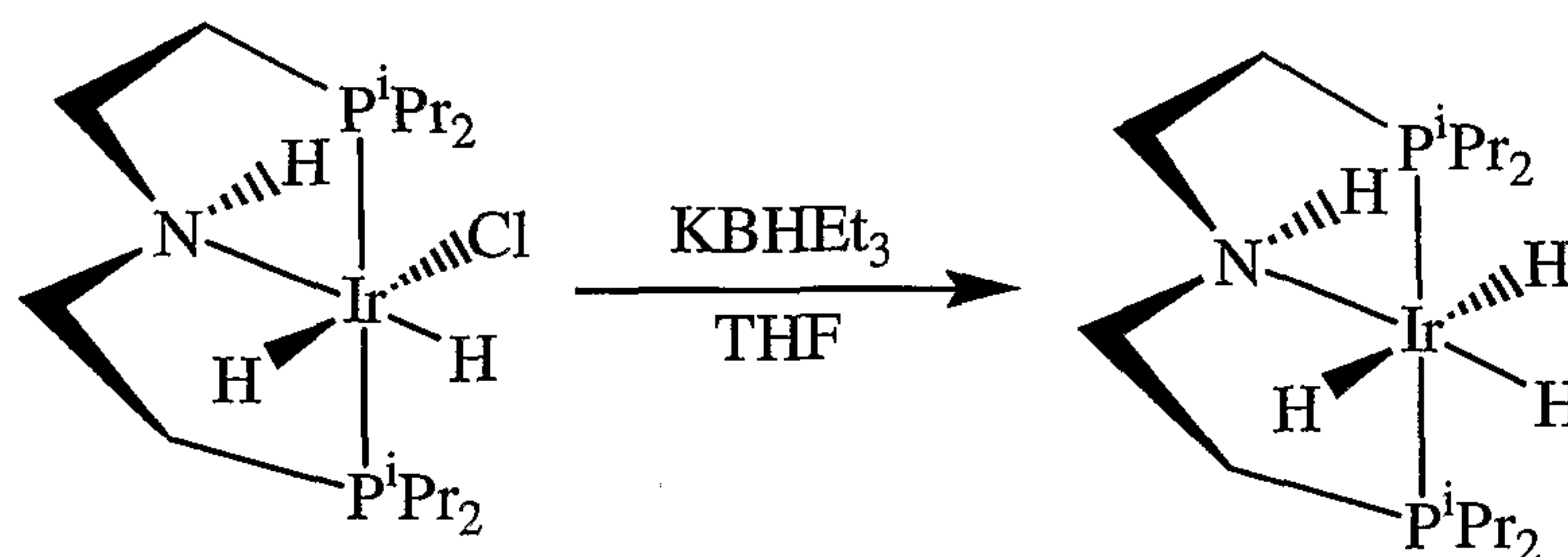
- 10 Chlorodiisopropylphosphine (11.0 g) was added in 2 g portions to a vigorously stirred suspension of lithium granules (1.5 g) in THF (30 ml) and the mixture was stirred for 3 days at room temperature. The mixture was filtered through a coarse sintered glass frit to remove excess lithium, then cooled to -80°C and a solution of $(\text{ClC}_2\text{H}_4)_2\text{NSiMe}_3$ (7.75 g) in 10 ml of THF slowly added. The resulting suspension
- 15 was allowed to slowly warm to room temperature and then refluxed for one hour. After cooling to room temperature, 15 ml of water was added and the mixture stirred for one hour. The aqueous layer was removed and another 15 ml of water and 15 ml of hexane added. The biphasic mixture was refluxed for 4 hours then cooled to room temperature. The aqueous layer was removed and the mixture evaporated to give the
- 20 crude diphosphine. This was purified by distillation under vacuum. The fraction boiling at $120\text{--}140^\circ\text{C}$ was collected. Yield = 9.72 g.

Example 1.2 Preparation of $\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$:

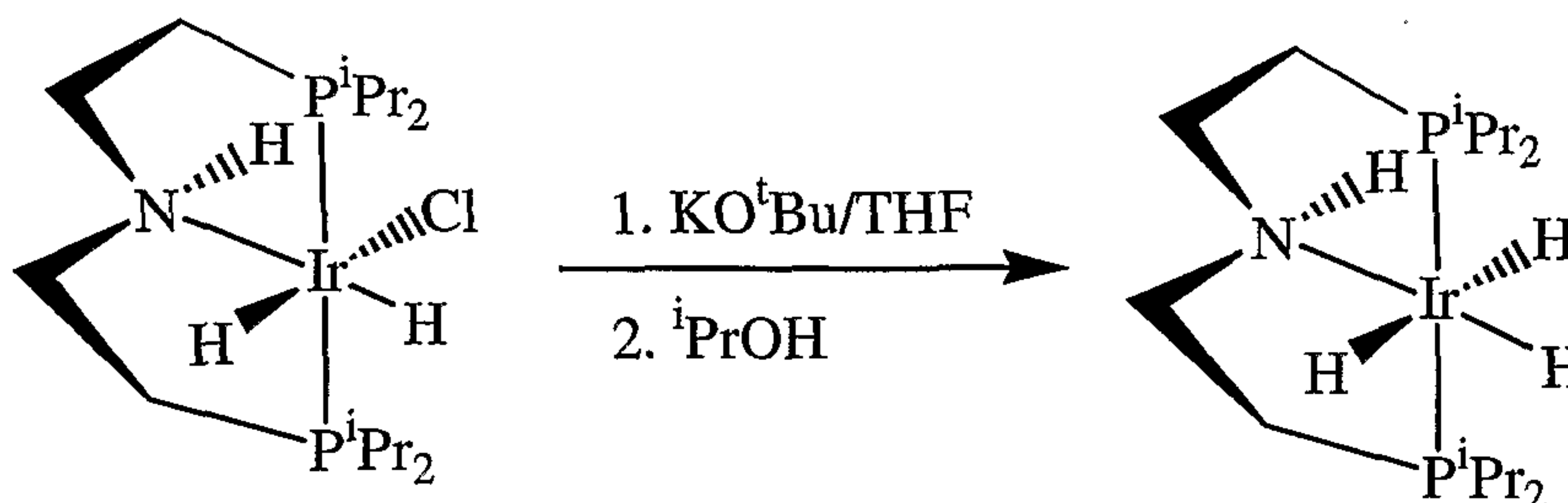


2-Propanol (3 ml) was added to a mixture of $[\text{Ir}(\text{coe})_2\text{Cl}]_2$ (1.5 g) and $(^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH}$ (1.02 g) and the mixture warmed for 45 minutes at 60°C. Hexane (6 ml) was added to the cooled solution, and the resulting crystalline white solid was filtered, washed with hexanes and dried under vacuum. Yield = 1.52 g. An X-ray crystal structure of this compound is shown in Figure 1.

Example 1.3 Preparation of $\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$



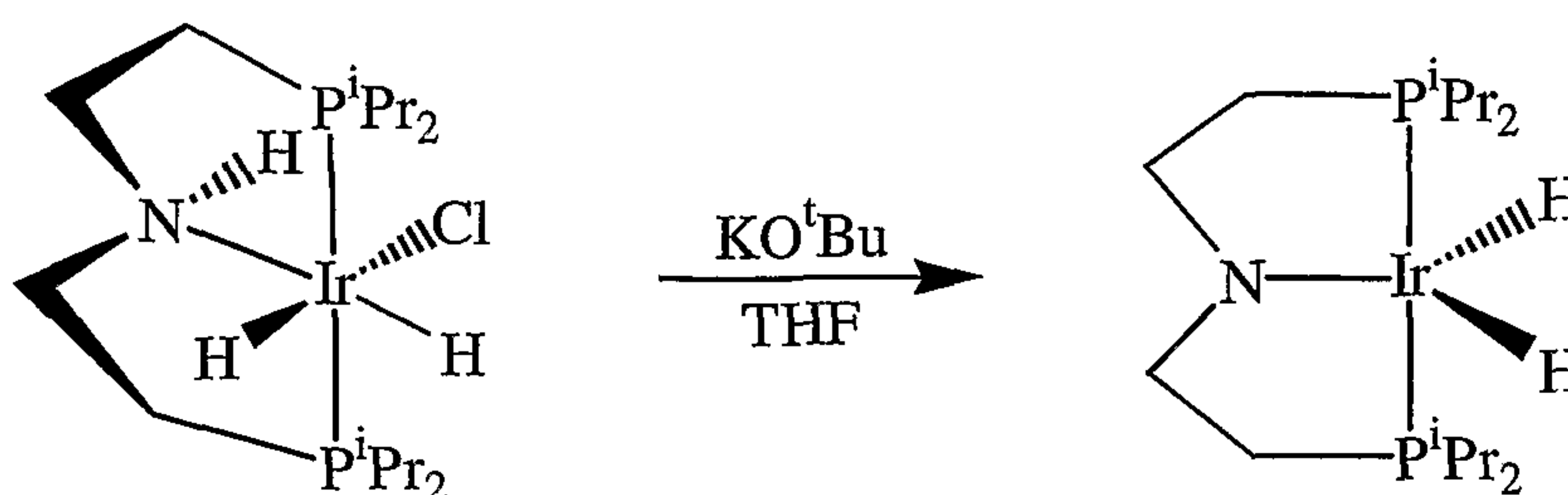
Method 1. A mixture of $\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ (800 mg) in THF (2 ml) and lithium triethylborohydride (1600 mg of a 1.0 M solution in THF) was stirred for 12 hours at room temperature. The mixture was evaporated to dryness and extracted with 3x10 ml toluene and filtered. The combined filtrate was evaporated to dryness, yielding the trihydride product as a viscous, colourless oil, which solidified after 10 days at room temperature, yielding a white solid. Yield = 628 mg.



Method 2. A mixture of $\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ (800 mg) in THF (5 ml) and KO^tBu (200 mg) was stirred for 10 minutes at room temperature. The mixture was filtered and 2-propanol (10 ml) added to the bright yellow solution, which immediately became colourless. The volume of the solvent was reduced to approximately 2 ml by evaporation under reduced pressure and hexane (10 ml) added. The crystalline white solid was filtered, washed with hexane and dried under vacuum. Yield = 715 mg.

Example 1.4 Preparation of $\text{IrH}_2((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{N})$

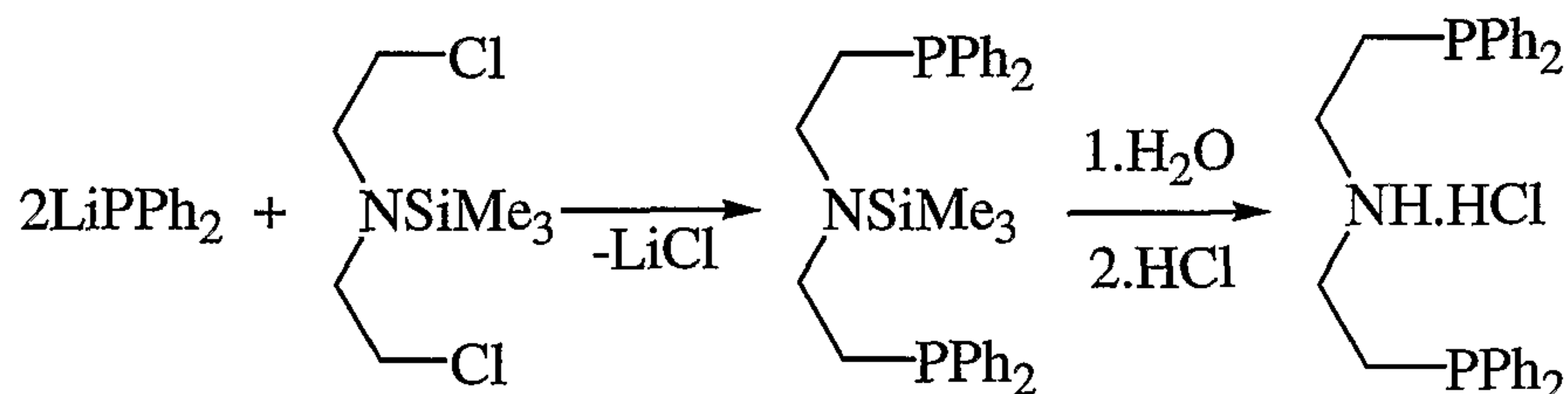
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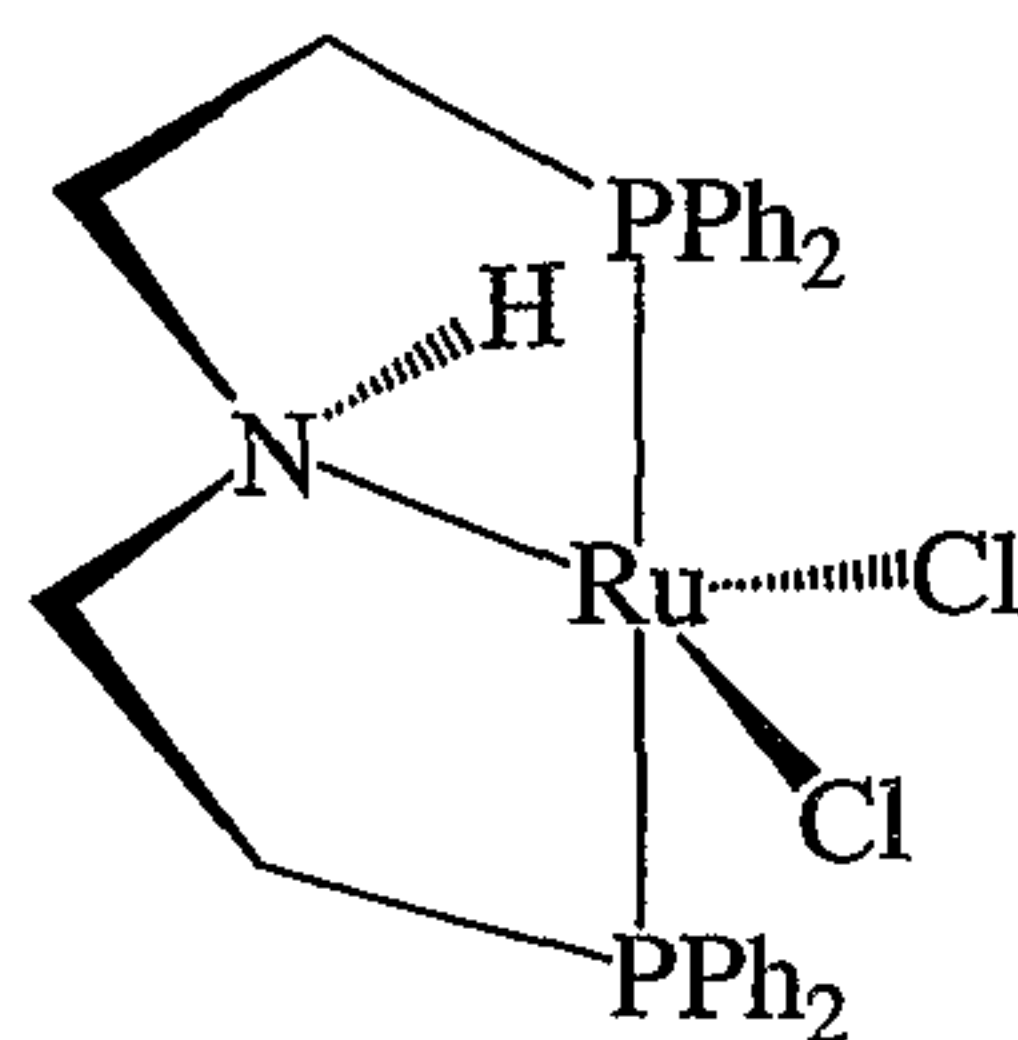
Tetrahydrofuran (2 ml) was added to a mixture of $\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ (250 mg) and KO^tBu (75 mg) and the mixture stirred for 30 minutes at room temperature. The mixture was filtered to remove KCl and excess base and the filtrate evaporated to near dryness. Hexane (5 ml) was then added and the suspension stirred for 1 hour. The yellow crystalline product was filtered, washed with hexane and dried under vacuum. Yield = 223 mg.

Example 2 : Preparation of the Ligand Bis(2-(diphenylphosphino)ethyl)amine, $(\text{Ph}_2\text{PC}_2\text{H}_4)_2\text{NH}$ and Metal Complexes

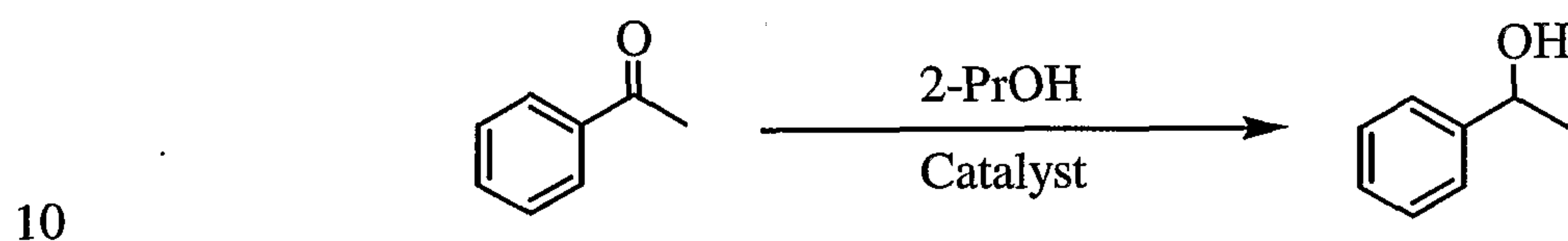
10 Example 2.1 Preparation of $(\text{Ph}_2\text{PC}_2\text{H}_4)_2\text{NH}\cdot\text{HCl}$



Chlorodiphenylphosphine (15.0 g) was added in 2 g portions to a vigorously stirred suspension of lithium granules (1.5 g) in THF (30 ml) and the mixture stirred for 3 days at room temperature. The mixture was cooled to -40°C and a solution of $(\text{ClC}_2\text{H}_4)_2\text{NSiMe}_3$ (8.5 g) in 10 ml of THF was slowly added. The resulting suspension was then allowed to slowly warm to room temperature and refluxed for one hour. After cooling to room temperature, 15 ml of water was added and the mixture stirred for one hour. The aqueous layer was removed and another 15 ml of water and 15 ml of hexane added. The biphasic mixture was refluxed for 4 hours then cooled to room temperature. The aqueous layer was removed and the mixture evaporated to give the crude diphosphine. A 2M solution of aqueous HCl (200 ml) was added with vigorous stirring, resulting in the formation of the ammonium chloride salt of the diphosphine as a white solid. This was washed with water, cold methanol and hexanes, then dried under vacuum. Yield = 14.32 g.

Example 2.2 Preparation of $\text{RuCl}_2((\text{Ph}_2\text{PC}_2\text{H}_4)_2\text{NH})$ 

2-Propanol (3 ml) was added to a mixture of $[\text{RuCl}_2(\text{benzene})]_2$ (250 mg), NEt_3 (200 mg) and $(\text{Ph}_2\text{PC}_2\text{H}_4)_2\text{NH}\cdot\text{HCl}$ (480 mg) and the mixture refluxed for 4 hours. The mixture was cooled to room temperature and the yellow solid filtered and washed with 2-propanol then dried under vacuum. Yield = 372 mg.

Example 3: Transfer hydrogenation of acetophenone using Iridium catalysts derived from Bis(2-(diisopropylphosphino)ethyl)amine, $(^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH}$ **Example 3.1 Transfer hydrogenation of acetophenone using $\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ as catalyst**

A weighed amount of $\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ is added to a solution of acetophenone in 2-propanol (ketone:2-PrOH approx. 1: 10) and the mixture stirred at the required temperature. The reaction progress is monitored using NMR. After attainment of an equilibrium conversion, the solvent is removed by evaporation under reduced pressure. A typical example is illustrated below:

$\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ (5 mg) is added to a solution of acetophenone (2.8 g) in 2-propanol (15 g) and the reaction mixture stirred for 1 hour at room temperature. The NMR of the reaction mixture showed 85 % conversion of the ketone to the alcohol. The solvent was evaporated under reduced pressure, resulting in > 99% phenyl ethanol. The results are presented in Table 1.

Example 3.2 Transfer hydrogenation of acetophenone using

$\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})/\text{KO}^t\text{Bu}$ as catalyst

A weighed amount of $\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ and KO^tBu (catalyst:base aprox. 1:10) is added to a solution of acetophenone in 2-propanol (ketone:2-PrOH approx. 1: 10) and the mixture stirred at the required temperature. The reaction progress is monitored using NMR. After attainment of an equilibrium conversion, the solvent is removed by evaporation under reduced pressure. A typical example is illustrated below:

5 $\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ (5 mg) and KO^tBu (10 mg) is added to a solution of acetophenone (2.8 g) in 2-propanol (15 g) and the reaction mixture stirred for 1 hour at room temperature. The NMR of the reaction mixture showed 84 % conversion of the ketone to the alcohol. The solvent was evaporated under reduced pressure,

10 resulting in > 99% phenyl ethanol. The results are presented in Table 2.

Example 3.3 Transfer hydrogenation of acetophenone using $\text{IrH}_2((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{N})$ as catalyst

A weighed amount of $\text{IrH}_2((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{N})$ is added to a solution of acetophenone in 2-propanol (ketone:2-PrOH approx. 1: 10) and the mixture stirred at the required

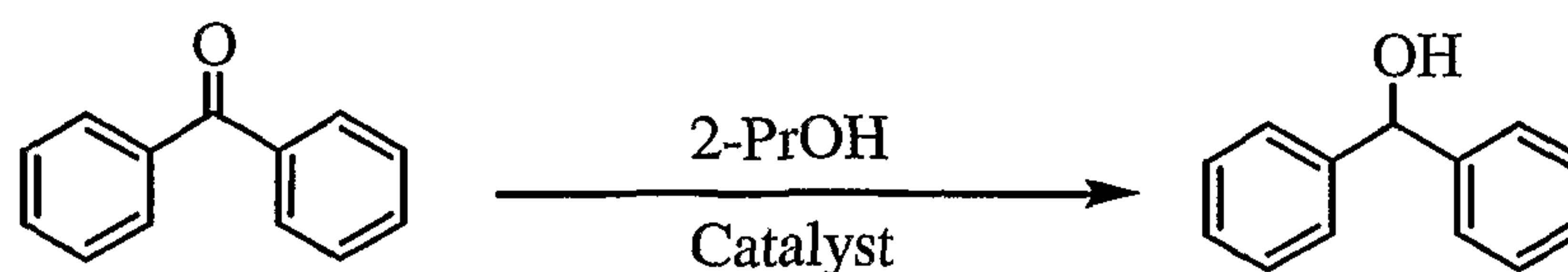
15 temperature. The reaction progress is monitored using NMR. After attainment of an equilibrium conversion, the solvent is removed by evaporation under reduced pressure. A typical example is illustrated below:

$\text{IrH}_2((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{N})$ (5 mg) is added to a solution of acetophenone (2.8 g) in 2-propanol (15 g) and the reaction mixture stirred for 1 hour at room temperature. The

20 NMR of the reaction mixture showed 82 % conversion of the ketone to the alcohol. The solvent was evaporated under reduced pressure, resulting in > 99% phenyl ethanol. The results are presented in Table 3.

Example 4.0: Transfer hydrogenation of benzophenone using Iridium catalysts derived from Bis(2-(diisopropylphosphino)ethyl)amine, $(^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH}$

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Example 4.1 Transfer hydrogenation of benzophenone using $\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ as catalyst

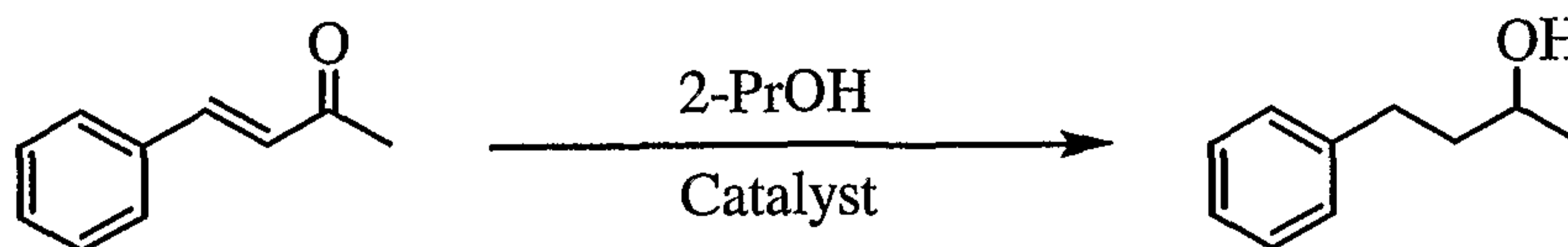
A weighed amount of $\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ is added to a solution of benzophenone in 2-propanol and the mixture stirred at the required temperature. The reaction progress is monitored using NMR. After attainment of an equilibrium conversion, the solvent is removed by evaporation under reduced pressure. A typical example is

5 illustrated below:
 $\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ (5 mg) is added to a solution of benzophenone (2.0 g) in 2-propanol (10 g) and the reaction mixture stirred for 1 hour at room temperature. The NMR of the reaction mixture showed 92 % conversion of the ketone to the alcohol. The solvent was evaporated under reduced pressure, resulting in > 99% benzhydrol.
 10 The results are presented in Table 4.

Example 4.2 Transfer hydrogenation of benzophenone using $\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})/\text{KO}^t\text{Bu}$ as catalyst

A weighed amount of $\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ and KO^tBu (catalyst:base aprox. 1:10) is added to a solution of benzophenone in 2-propanol (ketone:2-PrOH approx. 1: 10)
 15 and the mixture stirred at the required temperature. The reaction progress is monitored using NMR. After attainment of an equilibrium conversion, the solvent is removed by evaporation under reduced pressure. A typical example is illustrated below:
 $\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ (5 mg) and KO^tBu (10 mg) is added to a solution of benzophenone (2.0 g) in 2-propanol (10 g) and the reaction mixture stirred for 1 hour
 20 at room temperature. The NMR of the reaction mixture showed 91 % conversion of the ketone to the alcohol. The solvent was evaporated under reduced pressure, resulting in > 99% phenyl ethanol. The results are presented in Table 5

Example 5: Transfer hydrogenation of benzylidene acetone using Iridium catalysts derived from Bis(2-(diisopropylphosphino)ethyl)amine, $(^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH}$



Example 5.1 Transfer hydrogenation of benzylidene acetone using
 30 **$\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ as catalyst**

A weighed amount of $\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ is added to a solution of benzylidene acetone in 2-propanol and the mixture stirred at the required temperature. The reaction progress is monitored using NMR. After attainment of an equilibrium conversion, the solvent is removed by evaporation under reduced pressure. A typical example is illustrated below:

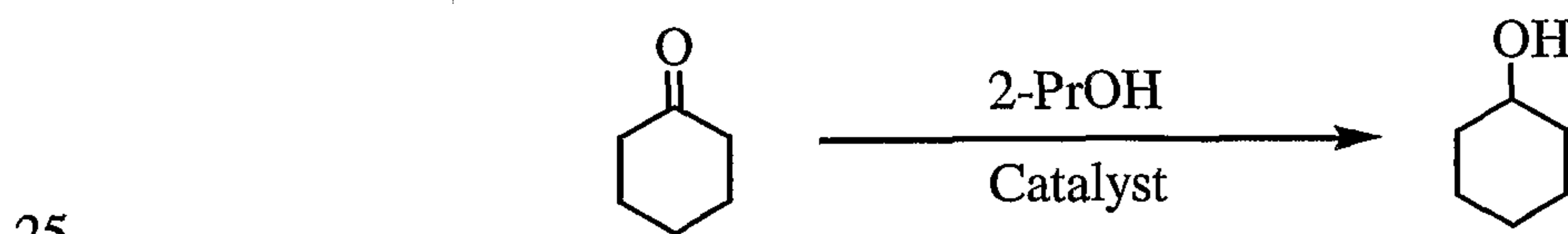
$\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ (5 mg) is added to a solution of benzylidene acetone (2.0 g) in 2-propanol (10 g) and the reaction mixture stirred for 1 hour at room temperature. The solvent was evaporated under reduced pressure, resulting in > 99% of the saturated alcohol. The results are presented in Table 6.

Example 5.2 Transfer hydrogenation of benzylidene acetone using $\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})/\text{KO}^t\text{Bu}$ as catalyst

A weighed amount of $\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ and KO^tBu (catalyst:base approx. 1:10) is added to a solution of benzylidene acetone in 2-propanol (ketone:2-PrOH approx. 1: 10) and the mixture stirred at the required temperature. The reaction progress is monitored using NMR. After attainment of an equilibrium conversion, the solvent is removed by evaporation under reduced pressure. A typical example is illustrated below:

$\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ (5 mg) and KO^tBu (10 mg) is added to a solution of benzylidene acetone (2.0 g) in 2-propanol (10 g) and the reaction mixture stirred for 1 hour at room temperature. The solvent was evaporated under reduced pressure, resulting in > 99% of the saturated alcohol. The results are presented in Table 7.

Example 6: Transfer hydrogenation of cyclohexanone using Iridium catalysts derived from Bis(2-(diisopropylphosphino)ethyl)amine, $(^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH}$



Example 6.1 Transfer hydrogenation of cyclohexanone using $\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ as catalyst

A weighed amount of $\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ is added to a solution of cyclohexanone in 2-propanol and the mixture stirred at the required temperature. The reaction

progress is monitored using NMR. After attainment of an equilibrium conversion, the solvent is removed by evaporation under reduced pressure. A typical example is illustrated below:

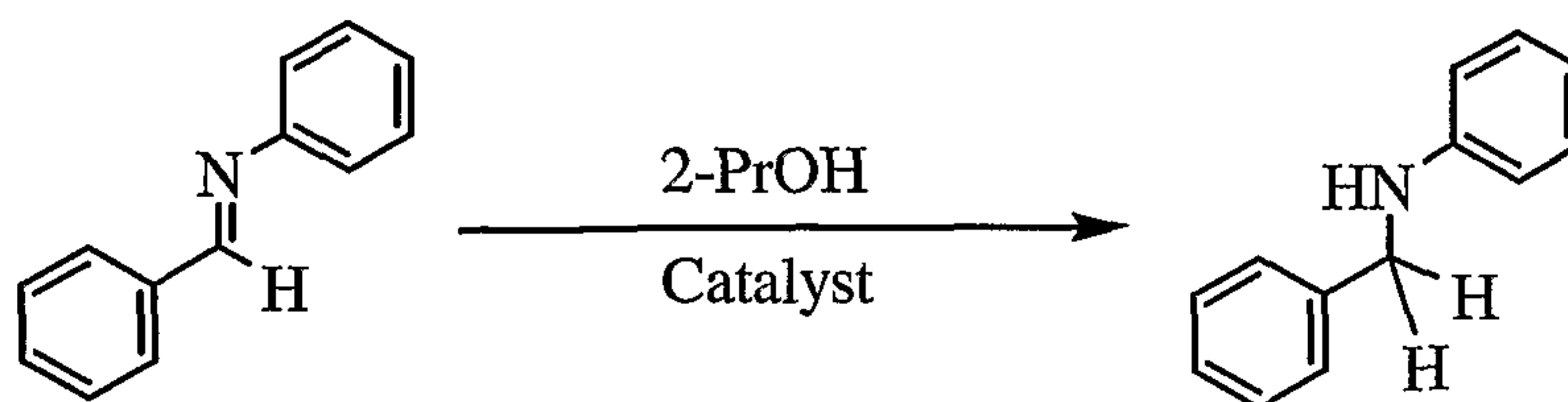
IrH₃((ⁱPr₂PC₂H₄)₂NH) (5 mg) is added to a solution of cyclohexanone (2.0 g) in 2-propanol (10 g) and the reaction mixture stirred for 1 hour at room temperature. The solvent was evaporated under reduced pressure, resulting in > 99% of the saturated alcohol. The results are presented in Table 8

Example 6.2 Transfer hydrogenation of cyclohexanone using IrH₂Cl((ⁱPr₂PC₂H₄)₂NH)/ KO^tBu as catalyst

A weighed amount of IrH₂Cl((ⁱPr₂PC₂H₄)₂NH) and KO^tBu (catalyst:base aprox. 1:10) is added to a solution of cyclohexanone in 2-propanol (ketone:2-PrOH approx. 1: 10) and the mixture stirred at the required temperature. The reaction progress is monitored using NMR. After attainment of an equilibrium conversion, the solvent is removed by evaporation under reduced pressure. A typical example is illustrated below:

IrH₂Cl((ⁱPr₂PC₂H₄)₂NH) (5 mg) and KO^tBu (10 mg) is added to a solution of cyclohexanone (2.0 g) in 2-propanol (10 g) and the reaction mixture stirred for 1 hour at room temperature. The solvent was evaporated under reduced pressure, resulting in > 99% of the saturated alcohol. The results are presented in Table 9.

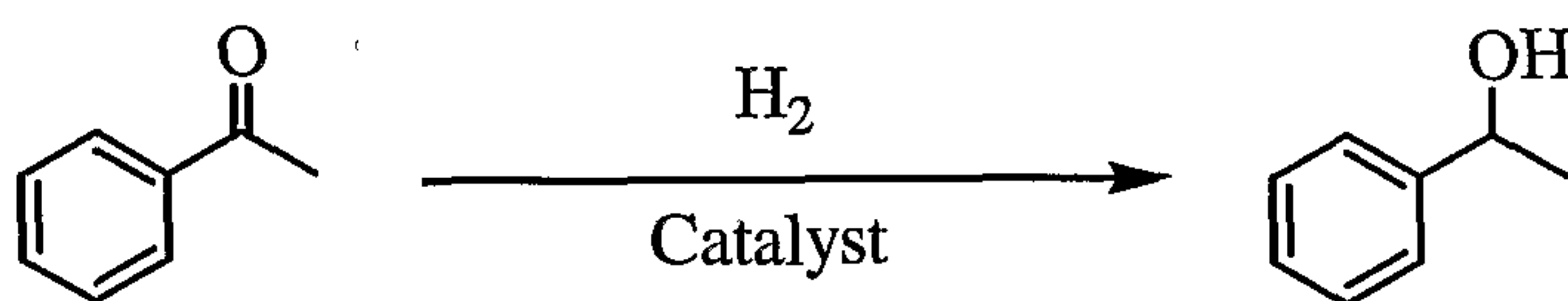
Example 7.0: Transfer hydrogenation N-(Benzylidene)phenylamine using Iridium catalysts derived from Bis(2-(diisopropylphosphino)ethyl)amine, (ⁱPr₂PC₂H₄)₂NH



A weighed amount of the catalyst is added to a solution of N-(Benzylidene)phenylamine in 2-propanol and the mixture stirred at the required temperature. The reaction progress is monitored using NMR. After attainment of an equilibrium conversion, the solvent is removed by evaporation under reduced pressure. A typical example is illustrated below:

$\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ (5 mg) is added to a solution of N-(Benzyldiene)phenylamine (1.5 g) in 2-propanol (10 g) and the reaction mixture stirred for 1 hour at 80°C. The solvent was evaporated under reduced pressure, to give the amine (93% yield). The results are presented in Table 10.

5 **Example 8.0 Hydrogenation of acetophenone using hydrogen gas and Iridium catalysts derived from Bis(2-(diisopropylphosphino)ethyl)amine, $(^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH}$**



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A weighed amount of the catalyst is added to a solution of acetophenone in benzene and the mixture stirred under hydrogen gas (3 atm) at the required temperature. The reaction progress was monitored using NMR. The results are presented in Table 11.

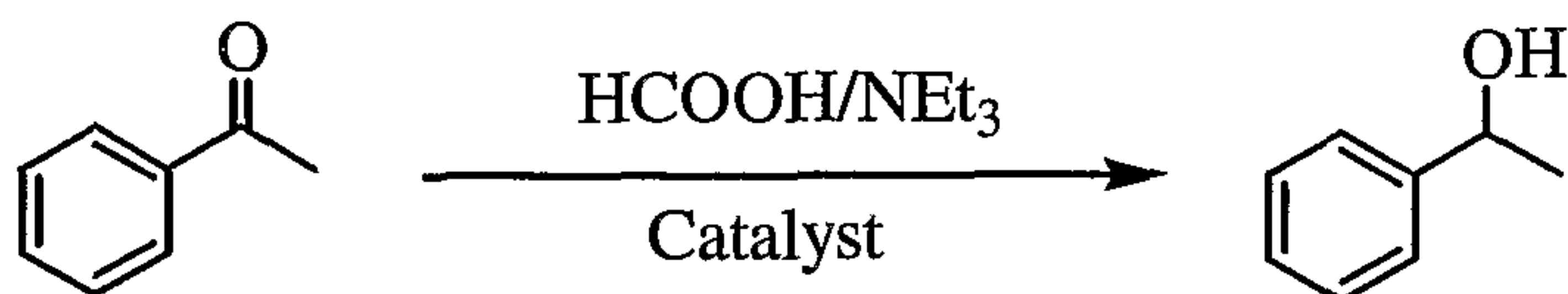
15 **Example 9 Transfer hydrogenation of ketones using an iridium catalyst generated in situ from $(\text{Ph}_2\text{PC}_2\text{H}_4)_2\text{NH}\cdot\text{HCl}$ (5 mg), $[\text{Ir}(\text{coe})_2\text{Cl}]_2$ (5 mg) and KO^tBu (10 mg)**

Weighed amounts of $[\text{Ir}(\text{coe})_2\text{Cl}]_2$, $(\text{Ph}_2\text{PC}_2\text{H}_4)_2\text{NH}\cdot\text{HCl}$ and KO^tBu are mixed together in an aliquot of 2-propanol. The required amount of the substrate and 2-propanol are then added and the mixture stirred at the required temperature for the
20 desired time. The reaction progress is monitored using NMR.

The transfer hydrogenation of acetophenone is illustrated below:

2-Propanol (1 ml) is added to a mixture of $(\text{Ph}_2\text{PC}_2\text{H}_4)_2\text{NH}\cdot\text{HCl}$ (5 mg), $[\text{Ir}(\text{coe})_2\text{Cl}]_2$ (5mg) and KO^tBu (10 mg) at room temperature in a 50 ml round bottom flask and the solution stirred for 10 minutes. Acetophenone (3.0 g) and 2-propanol (12 g) are then
25 added and the reaction mixture stirred for 1 hour at 60°C. The results are presented in Table 12.

Example 10: Transfer hydrogenation of acetophenone using HCOOH/NEt₃ and an iridium catalyst generated in situ from (Ph₂PC₂H₄)₂NH.HCl, [Ir(coe)₂Cl]₂ and KO^tBu



- 5 Triethylammonium formate (1.0 g HCOOH/NEt₃, 5:2) is added to a mixture of (Ph₂PC₂H₄)₂NH.HCl (5 mg), [Ir(coe)₂Cl]₂ (5mg), KO^tBu (10 mg) and acetophenone (1.0 g) and the resulting solution stirred for 8 hours at 60°C. the NMR spectrum of the reaction mixture showed 75% conversion of the ketone to phenyl ethanol.

Example 11: Transfer hydrogenation of acetophenone using a rhodium catalyst generated in situ from (iPr₂PC₂H₄)₂NH, [Rh(cod)Cl]₂ and KO^tBu

- 10 2-Propanol (1 ml) is added to a mixture of (iPr₂PC₂H₄)₂NH (15 mg), [Rh(cod)Cl]₂ (10mg) and KO^tBu (10 mg) at room temperature in a 50 ml round bottom flask and the solution stirred for 10 minutes. Acetophenone (1.5 g) and 2-propanol (7.5 g) are then added and the reaction mixture stirred for 1 hour at 80°C. The NMR of the
15 reaction mixture showed 82% conversion of the ketone to phenyl ethanol.

Example 12: Transfer hydrogenation of acetophenone using a ruthenium catalyst

- 2-Propanol (10 ml) is added to a mixture of RuCl₂[(Ph₂PC₂H₄)₂NH] (10 mg), acetophenone (2.0 g) and KO^tBu (10 mg) and the reaction mixture stirred for 1 hour
20 at 80°C. The NMR of the reaction mixture showed 79% conversion of the ketone to phenyl ethanol.

Example 13: Catalytic hydrogenation of ketones and imines with Ruthenium Catalysts

- In a typical catalytic hydrogenation procedure, weighed amounts of the catalyst and
25 KO^tBu are added to a solution of the neat substrate or its solution in 2-propanol and the mixture is then stirred at the required temperature under 3 atm of H₂ gas. The reaction progress is monitored using NMR.

The hydrogenation of acetophenone is illustrated below:

- The catalyst (10 mg) and KO^tBu (10 mg) is added to a solution of neat acetophenone
30 (1.0 g) and the reaction mixture stirred for 3 hours at room temperature. The proton

NMR spectrum of the reaction mixture showed 100 % conversion of the ketone to the alcohol. The results are shown in Table 13.

Example 14: Hydrogenation Reactions Using an In Situ Generated Ruthenium Catalyst

- 5 In a typical catalytic hydrogenation procedure using an in situ generated ruthenium catalyst, weighed amounts of $[\text{RuCl}_2(\text{benzene})]_2$, the ligand and KO^tBu are mixed together in an aliquot of toluene. The required amount of the substrate and 2-propanol are then added and the mixture stirred at the required temperature for the desired time under an atmosphere of hydrogen gas. The hydrogenation of acetophenone is
10 illustrated below:

A weighed amount of $(\text{Ph}_2\text{PC}_2\text{H}_4)_2\text{NH}$ (10 mg), $[\text{RuCl}_2(\text{benzene})]_2$ (10mg) and KO^tBu (10 mg) in toluene (1 ml) are mixed together at room temperature in a round bottom flask. Acetophenone (2.0 g) and 2-propanol (2 g) are then added and the reaction mixture stirred for 1 hour at room temperature under hydrogen gas (3 atm).

- 15 The NMR spectrum shows complete conversion of the ketone after 3 hours.
The results are shown in Table 14.

While the present invention has been described with reference to what are presently considered to be the preferred examples, it is to be understood that the invention is not limited to the disclosed examples. To the contrary, the invention is
20 intended to cover various modifications and equivalent arrangements included within the spirit and scope of the appended claims.

Table 1: Performance of $\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ as catalyst for the transfer hydrogenation of acetophenone.

Run	Temp/ $^{\circ}\text{C}$	Mass Substrate	Mass Catalyst	S:C Ratio	Time	Yield / %
1	25	2.8 g	5 mg	2,300	1 hr	>99
2	25	5.6 g	5 mg	4,600	2 hr	>99
3	60	11.2 g	5 mg	9,200	1 hr	96
4	60	22.5 g	5 mg	19,000	2 hr	97
5	60	45 g	5 mg	38,000	5 hr	94

Table 2: Performance of $\text{IrH}_2\text{Cl}(\text{iPr}_2\text{PC}_2\text{H}_4)_2\text{NH})/\text{KO}^t\text{Bu}$ as catalyst for the transfer hydrogenation of acetophenone.

Run	<i>Temp/°C</i>	Mass Substrate	Mass Catalyst	S:C Ratio	Time	Yield / %
1	25	2.8 g	5 mg	2,300	1 hr	>99
2	25	5.6 g	5 mg	4,600	2 hr	>99
3	60	11.2 g	5 mg	9,200	1 hr	98

Table 3: Performance of $\text{IrH}_2((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{N})$ as catalyst for the transfer hydrogenation of acetophenone.

Run	<i>Temp/°C</i>	Mass Substrate	Mass Catalyst	S:C Ratio	Time	Yield / %
1	25	2.8 g	5 mg	2,300	1 hr	>99
2	25	5.6 g	5 mg	4,600	2 hr	>99

Table 4: Performance of $\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ as catalyst for the transfer hydrogenation of benzophenone.

Run	<i>Temp/°C</i>	Mass Substrate	Mass Catalyst	S:C Ratio	Time	Yield / %
1	25	2.0 g	5 mg	1,100	10 min	>99
2	25	16.5 g	5 mg	9,100	2.5 hr	>99
3	25	30.0 g	3 mg	27,500	overnight	>99

Table 5: Performance of $\text{IrH}_2\text{Cl}(\text{iPr}_2\text{PC}_2\text{H}_4)_2\text{NH})/\text{KO}^t\text{Bu}$ as catalyst for the transfer hydrogenation of benzophenone.

Run	<i>Temp/°C</i>	Mass Substrate	Mass Catalyst	S:C Ratio	Time	Yield / %
1	25	2.0 g	5 mg	1,100	1 hr	>99
2	25	16.5 g	5 mg	9,100	2.5 hr	>99

Table 6: Performance of $\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ as catalyst for the transfer hydrogenation of benzylidene acetone.

Run	<i>Temp/°C</i>	Mass Substrate	Mass Catalyst	S:C Ratio	Time	Yield / %
1	25	2.0 g	5 mg	1,400	1 hr	>99
2	25	5.0 g	5 mg	3,400	2 hr	>99

Table 7: Performance of $\text{IrH}_2\text{Cl}(\text{iPr}_2\text{PC}_2\text{H}_4)_2\text{NH})/\text{KO}^t\text{Bu}$ as catalyst for the transfer hydrogenation of benzylidene acetone.

Run	<i>Temp/°C</i>	Mass Substrate	Mass Catalyst	S:C Ratio	Time	Yield / %
1	25	2.0 g	5 mg	1,400	1 hr	>99
2	25	5.0 g	5 mg	3,400	2 hr	>99

Table 8: Performance of $\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$ as catalyst for the transfer hydrogenation of cyclohexanone.

Run	<i>Temp/°C</i>	Mass Substrate	Mass Catalyst	S:C Ratio	Time	Yield / %
1	25	2.0 g	5 mg	2,000	10 min	>99
2	25	5.0 g	5 mg	5,000	1 hr	>99

Table 9: Performance of $\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})/\text{KO}^t\text{Bu}$ as catalyst for the transfer hydrogenation of cyclohexanone.

Run	<i>Temp/°C</i>	Mass Substrate	Mass Catalyst	S:C Ratio	Time	Yield / %
1	25	2.0 g	5 mg	2,000	1 hr	>99
2	25	5.0 g	5 mg	5,000	1 hr	>99

Table 10: Performance of Iridium complexes as catalyst for the transfer hydrogenation of N-(Benzylidene)phenylamine.

Catalyst	<i>Temp/°C</i>	Mass Substrate	Mass Catalyst	S:C Ratio	Time	Yield / %
$\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$	80	1.5 g	5 mg	800	1 hr	93
$\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})/\text{KO}^t\text{Bu}$	80	1.0 g	5 mg	550	1 hr	96
$\text{IrH}_2((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{N})$	80	1.0 g	5 mg	550	1 hr	94

Table 11: Performance of Iridium catalysts for the hydrogenation of acetophenone.

Catalyst	<i>Temp/°C</i>	Mass Substrate	Mass Catalyst	S:C Ratio	Time	Yield / %
$\text{IrH}_3((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})$	25	1.0 g	5 mg	800	12 hr	0
$\text{IrH}_2\text{Cl}((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{NH})/\text{KO}^t\text{Bu}$	25	1.0 g	5 mg	800	12 hr	<1
$\text{IrH}_2((^i\text{Pr}_2\text{PC}_2\text{H}_4)_2\text{N})$	25	1.0 g	5 mg	800	12 hr	0

Table 12: Performance of in situ generated iridium catalyst for the transfer hydrogenation of ketones using $(\text{Ph}_2\text{PC}_2\text{H}_4)_2\text{NH}\cdot\text{HCl}$ (5 mg), $[\text{Ir}(\text{coe})_2\text{Cl}]_2$ (5 mg) and KO^tBu (10 mg).

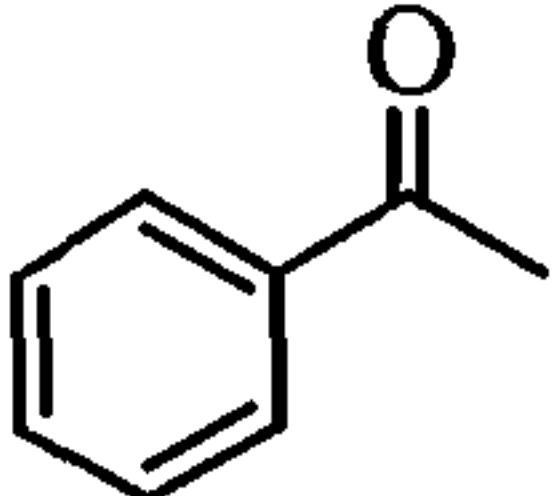
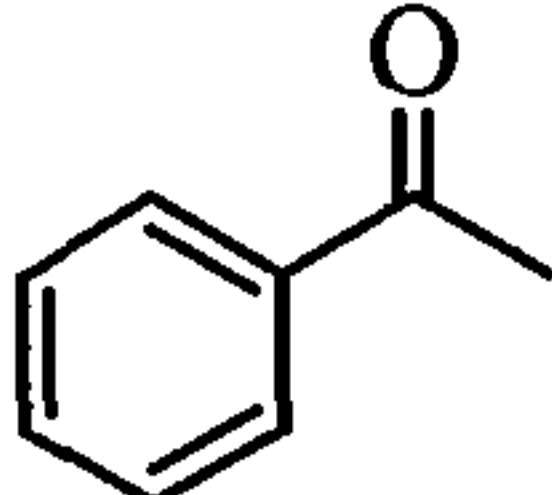
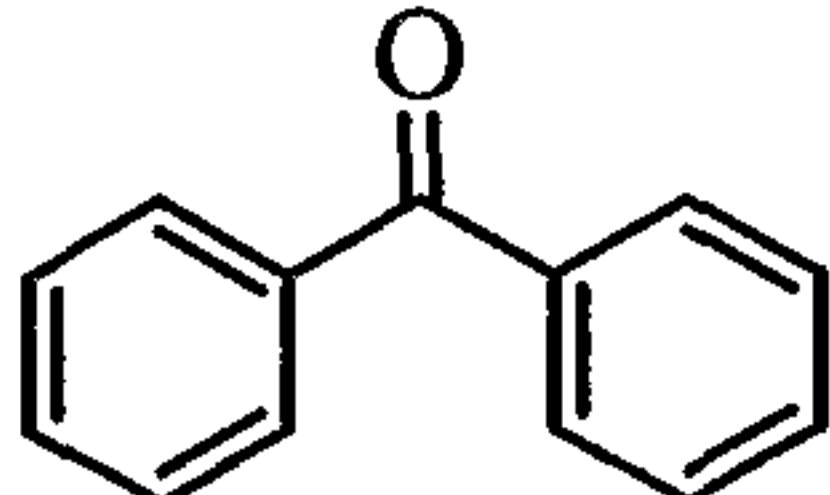
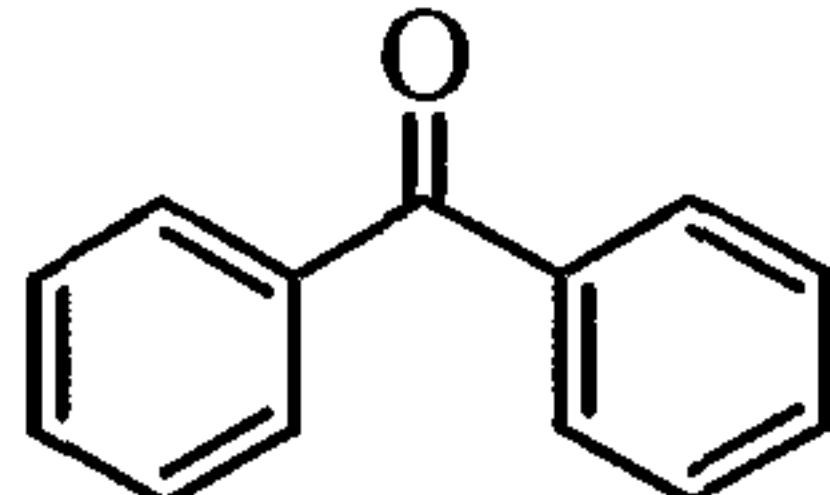
Substrate	Temp/ $^{\circ}\text{C}$	Mass Substrate	Mass 2-PrOH	Time	Conv. %
	60	1.0 g	5 g	20 min	81
	60	3.0 g	12 g	1 hour	82
	60	1.0 g	5 g	20 min	94
	60	3.0 g	12 g	1 hour	93

Table 13: Performance of $\text{RuCl}_2(\text{PPh}_2\text{PC}_2\text{H}_4)_2\text{NH}$ as catalyst for the hydrogenation of various ketones and imines.

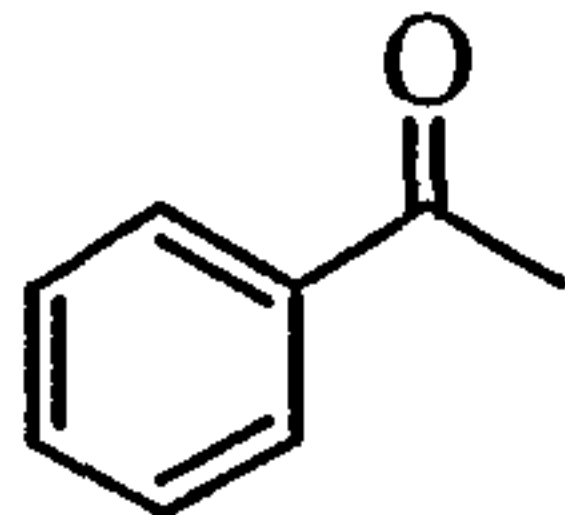
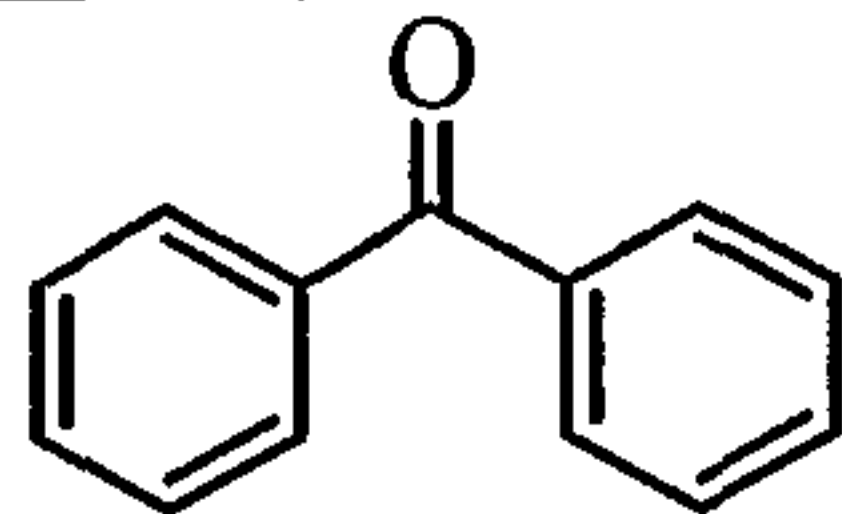
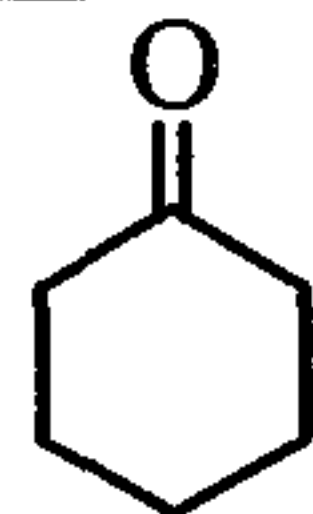
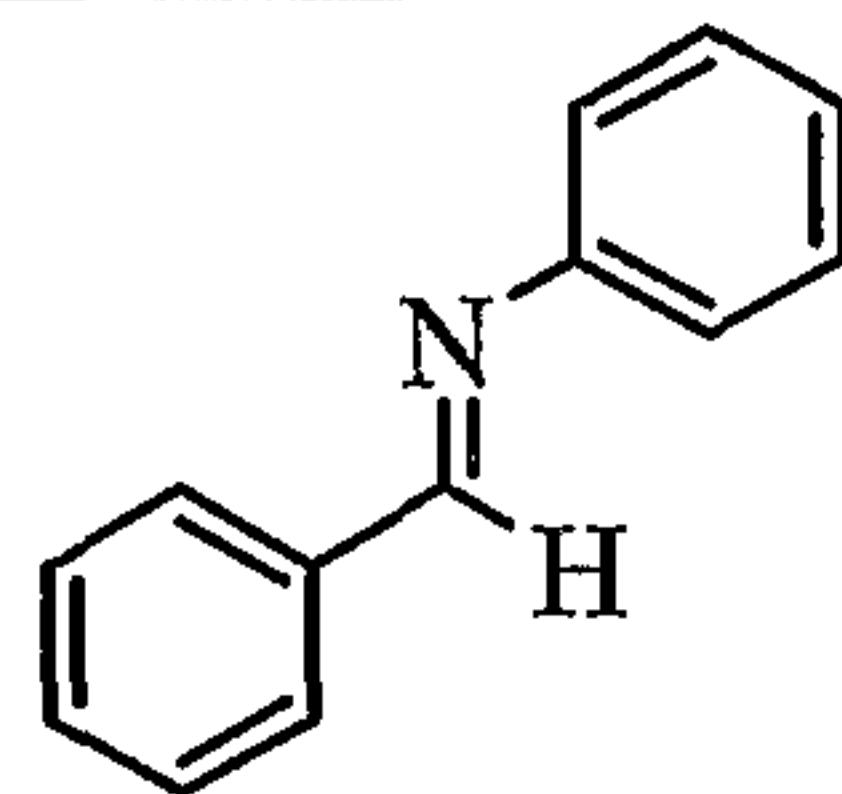
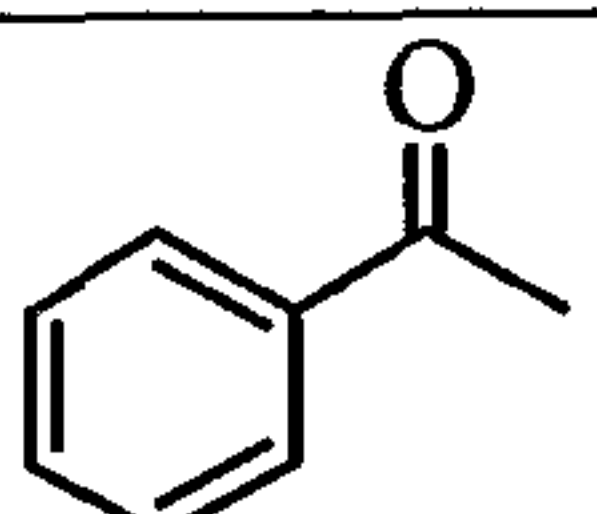
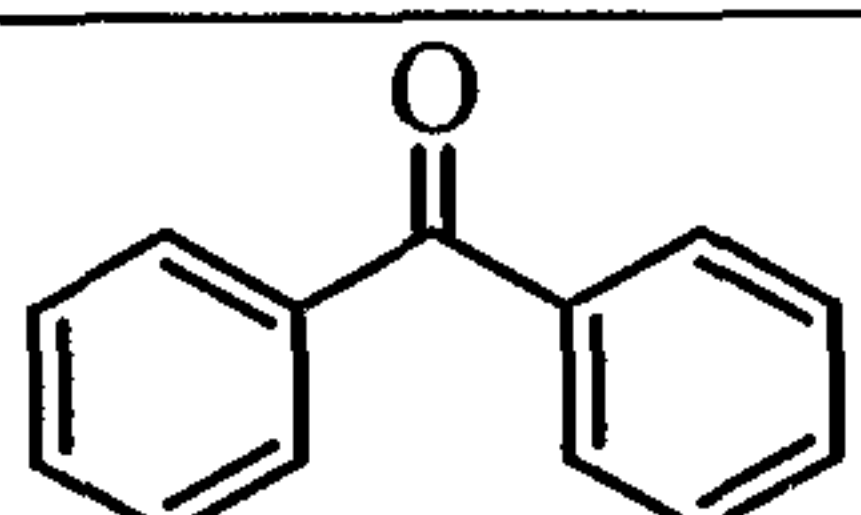
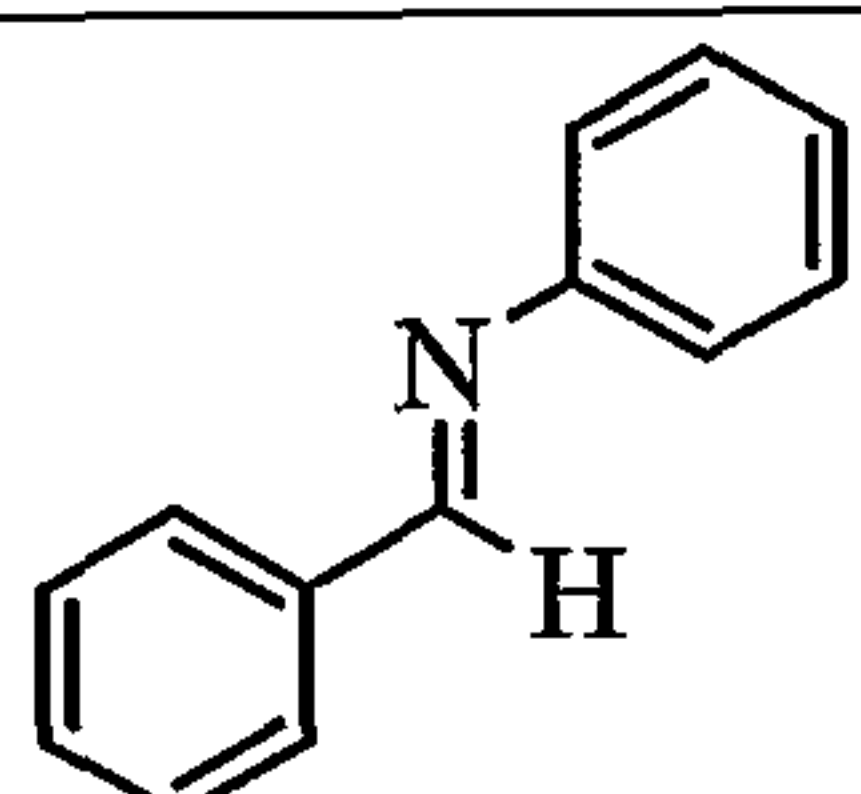
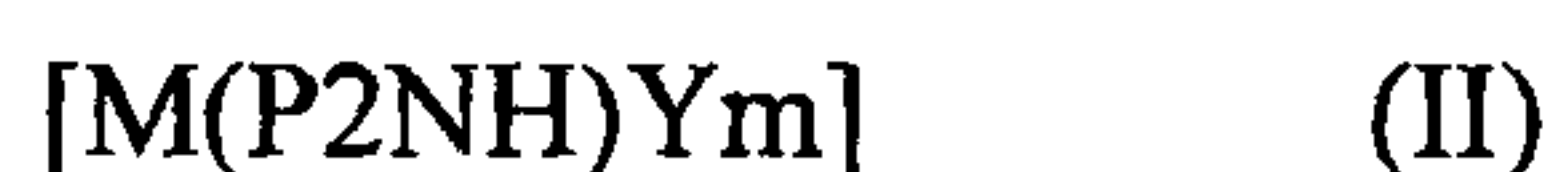
Substrate	Temp/ $^{\circ}\text{C}$	Mass Substrate	Mass Catalyst	Time	Isolated Yield /%
	25	1.0 g	10 mg	3 hr	100
	25	2.0 g	10 mg	3 hr	100
	25	2.0 g	10 mg	3 hr	100
	25	1.5 g	10 mg	1 hr	100

Table 14: Performance of in situ generated ruthenium catalyst for the hydrogenation of ketones using $(\text{Ph}_2\text{PC}_2\text{H}_4)_2\text{NH}\cdot\text{HCl}$ (10 mg), $[\text{RuCl}_2(\text{benzene})]_2$ (10 mg) and KO^tBu (5 mg).

Substrate	Temp/ $^{\circ}\text{C}$	Mass Substrate	Mass 2-PrOH	Time	Conv. %
	25	2.0 g	2 g	3 hr	100
	25	2.0 g	2 g	3 hr	100
	25	1.0 g	2 g	3 hr	100

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A process for the reduction of compounds comprising a carbon-carbon (C=C), carbon-oxygen (C=O), or carbon-nitrogen (C=N) double bond, to a corresponding hydrogenated alkane, alcohol or amine, comprising contacting a compound comprising the C=C, C=O or C=N double bond with a hydrogen donor and a catalyst comprising a metal complex having a tridentate aminodiphosphine ligand under transfer hydrogenation conditions, wherein the catalyst comprises a metal complex with a tridentate aminodiphosphine ligand of the formula (II)



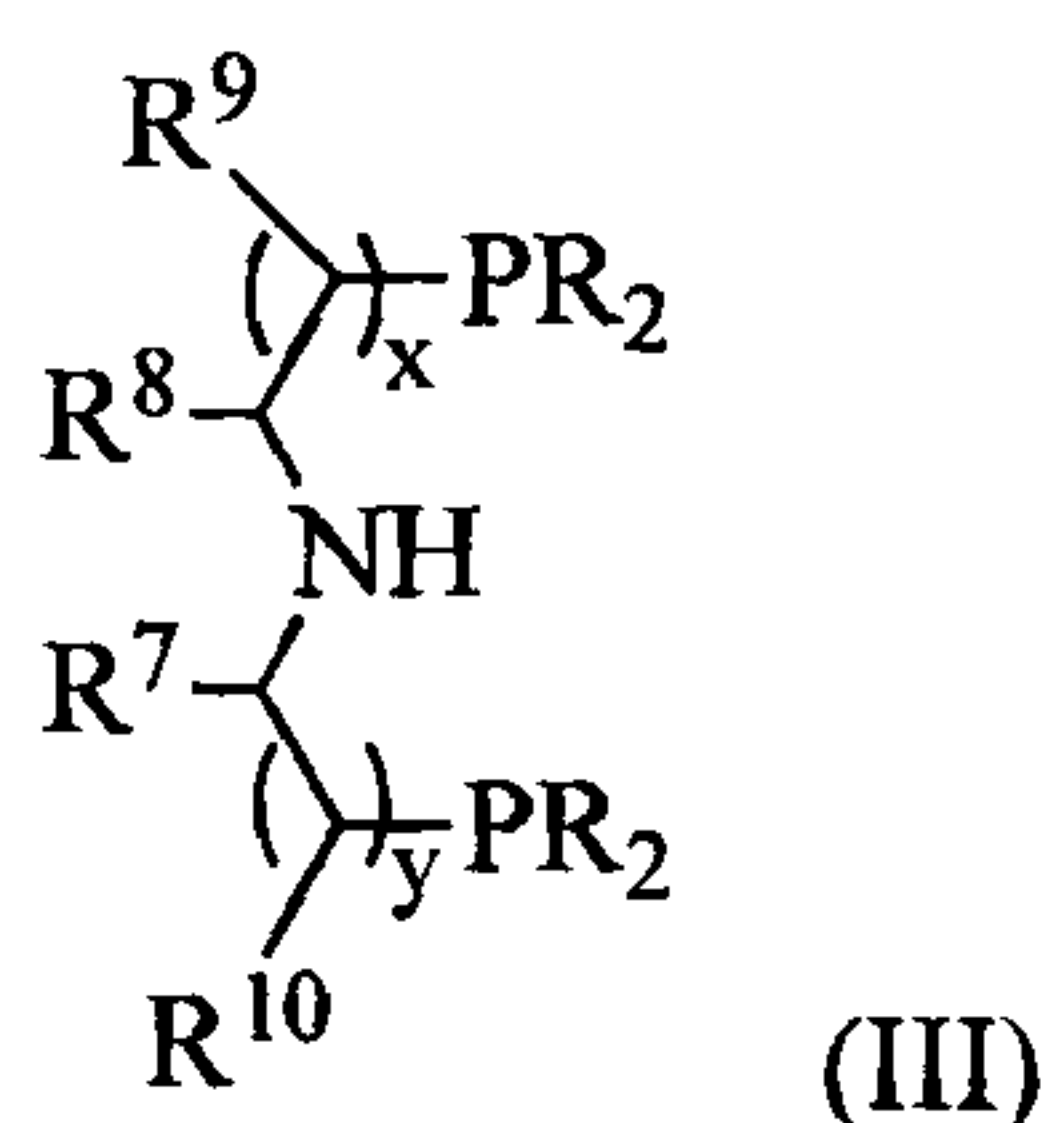
wherein

M is a metal;

Y simultaneously or independently are any anionic or neutral ligand;

m is an integer representing the number of ligands Y that are required to fulfill the valency requirements of M; and

the ligand (P₂NH) represents a tridentate aminodiphosphine ligand of formula (III):



in which R⁷ to R¹⁰ simultaneously or independently are selected from the group consisting of H, C₁₋₂₀alkyl, C₂₋₂₀alkenyl, C₃₋₂₀cycloalkyl and aryl, said latter 4 groups being optionally substituted, or two adjacent or geminal groups are bonded together to form an optionally substituted ring;

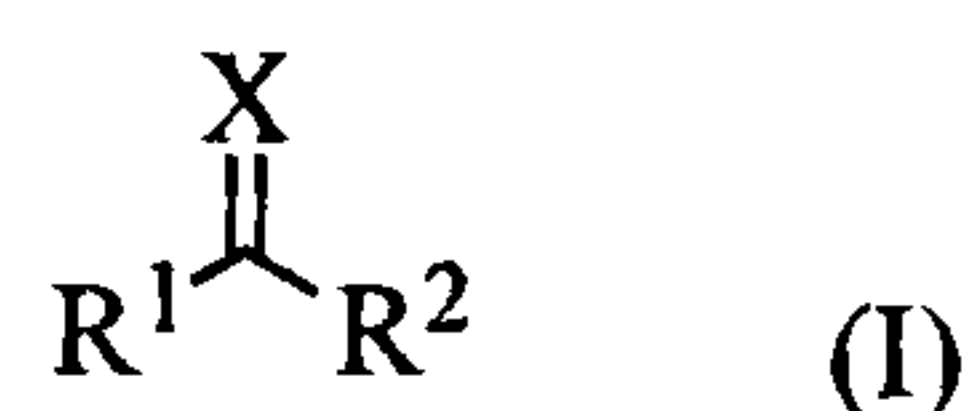
x and y are, simultaneously or independently, equal to 0, 1, 2, 3 or 4; and

R is simultaneously or independently selected from the group consisting of H, C₁₋₂₀alkyl, aryl and C₂₋₂₀alkenyl, OR and NR₂, said latter 5 groups being optionally substituted, or the R groups

on the same P atom may be linked together to form an optionally substituted monocyclic or polycyclic ring system having 4 or more atoms, including the phosphorous atom to which said R groups are bonded, which is saturated, unsaturated and/or aromatic and in which one or more carbon atoms in said monocyclic or polycyclic ring system may optionally be replaced with a heteroatom selected from O, S, N, and Si,

wherein the optional substituents are selected from one or more of halo, OH, NH₂, OR^c, NR^c₂ and R^c, in which R^c is selected from the group consisting of C₁₋₆alkyl, C₂₋₆alkenyl and aryl, and wherein the catalyst further optionally comprises a base.

2. The process according to claim 1, wherein the compound comprising a carbon-carbon (C=C), carbon-oxygen (C=O) or carbon-nitrogen (C=N) double bond is a compound of formula (I):



wherein,

X is selected from the group consisting of CR³R⁴, NR⁵, (NR⁵R⁶)⁺Q⁻ and O;

R¹ and R² each simultaneously or independently are selected from the group consisting of H, aryl, C₁₋₂₀alkyl, C₂₋₂₀alkenyl, C₃₋₂₀cycloalkyl and heteroaryl, said latter 5 groups being optionally substituted, or R¹ and R² are linked to form an optionally substituted ring;

R³ to R⁶ each independently or simultaneously are selected from the group consisting of H, OH, C₁₋₂₀alkoxy, aryloxy, C₁₋₂₀alkyl, C₂₋₂₀alkenyl, C₃₋₂₀cycloalkyl and aryl, said latter 6 groups being optionally substituted, or one or more of R¹ to R⁶ are linked to form an optionally substituted ring or rings; and

Q⁻ represents an anion,

wherein heteroaryl is a mono- or bicyclic heteroaromatic radical containing from 5 to 10 atoms, of which 1-3 atoms may be a heteroatom selected from the group consisting of S, O and N, and wherein the optional substituents are selected from the group consisting of halo, OH, NH₂, OR^c, NR^c₂ and R^c, in which R^c is selected from the group consisting of C₁₋₆alkyl, C₂₋₆alkenyl and aryl and one or more of the carbon atoms in the alkyl, alkenyl and cycloalkyl groups may be optionally replaced with a heteroatom selected from the group consisting of O, S, N, P or Si.

3. The process according to claim 2, wherein R^1 and R^2 are different.

4. The process according to any one of claims 1-3, wherein in the tridentate ligand of formula III, R^7 to R^{10} simultaneously or independently are selected from the group consisting of

5 H,

C_{1-10} alkyl, C_{2-10} alkenyl, C_{3-10} cycloalkyl and aryl, said latter 4 groups being optionally substituted, or two adjacent or geminal groups are bonded together to form an optionally substituted ring.

10 5. The process according to claim 4, wherein R^7 to R^{10} simultaneously or independently are selected from the group consisting of H, C_{1-4} alkyl, C_{2-4} alkenyl, C_{3-6} cycloalkyl and aryl, said latter 4 groups being optionally substituted, or two adjacent or geminal groups are bonded together to form an optionally substituted ring, said ring containing 6 atoms, including the carbons to which said groups are attached.

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6. The process according to claim 5, wherein R^7 to R^{10} are all H.

7. The process according to any one of claims 1-6, wherein x and y are simultaneously equal to 0, 1, 2, 3 or 4.

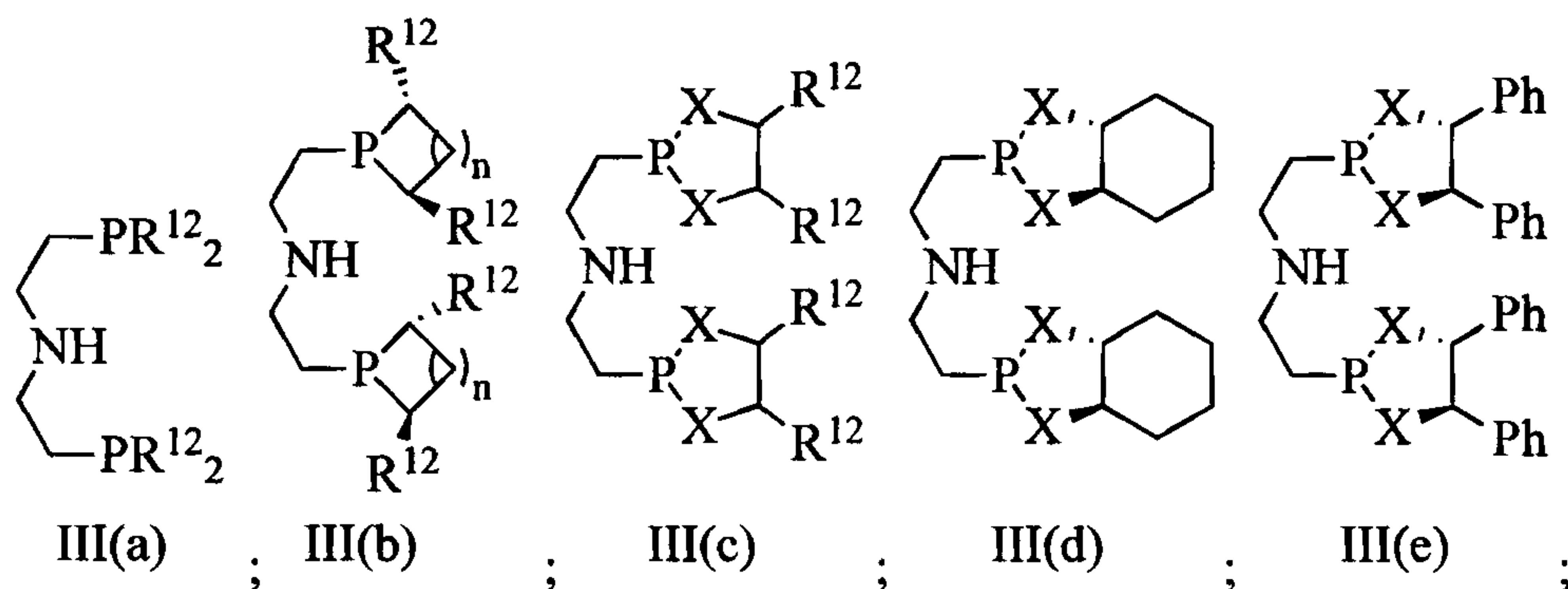
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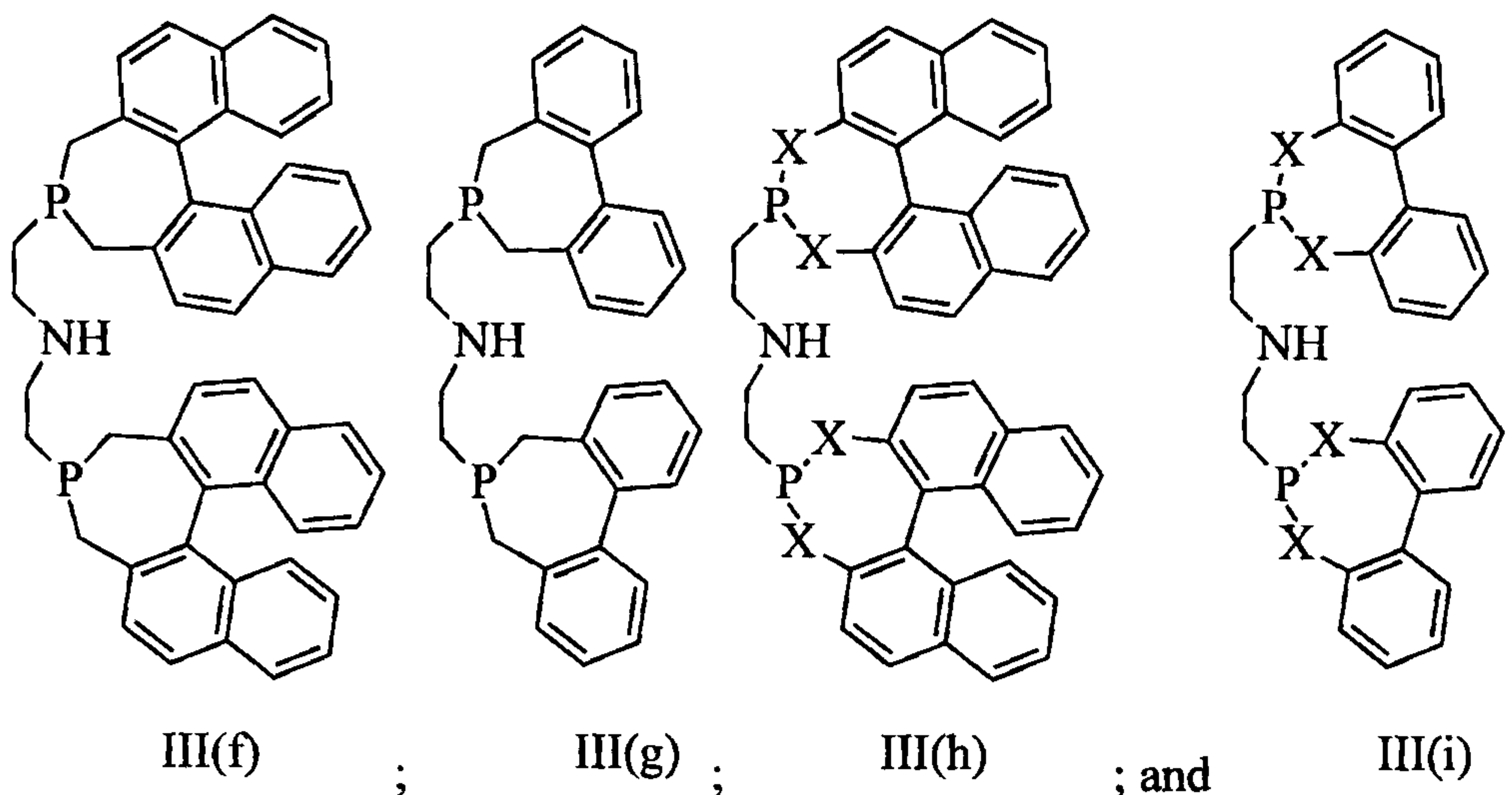
8. The process according to claim 7, wherein x and y are simultaneously equal to 0, 1 or 2.

9. The process according to claim 8, wherein x and y are simultaneously equal to 1.

25 10. The process according to any one of claims 1-9, wherein in the tridentate ligand of formula III, R is simultaneously or independently selected from the group consisting of H, C_{1-10} alkyl, aryl and C_{2-10} alkenyl, said latter 3 groups being optionally substituted, or the R groups on the same P atom may be linked together to form an optionally substituted monocyclic or polycyclic ring system having 4 or more atoms, including the phosphorous atom to which said R
30 groups are bonded, which is saturated, unsaturated and/or aromatic and in which one or more carbon atoms in said monocyclic or polycyclic ring system may optionally be replaced with a heteroatom selected from O and NH.

11. The process according to claim 10, wherein R is simultaneously or independently selected from the group consisting of H, C₁₋₆alkyl, phenyl, naphthyl and C₂₋₆alkenyl, said latter 3 groups being optionally substituted, or the R groups on the same P atom may be linked together to form an optionally substituted monocyclic, fused bicyclic, fused tricyclic, fused quadracyclic or fused pentacyclic ring system having 4-23 atoms, including the phosphorous atom to which said R groups are bonded, which is saturated, unsaturated and/or aromatic and in which one or more carbon atoms in said monocyclic or polycyclic ring system may optionally be replaced with a heteroatom selected from O and NH.
12. The process according to claim 11, wherein R is simultaneously C₁₋₆alkyl or phenyl.
13. The process according to any one of claims 1-12, the optional substituents on the compounds of formula III are selected from one or more of halo, OH, NH₂, OR^c, NR^c₂ and R^c, in which R^c is selected from the group consisting of C₁₋₄alkyl, C₂₋₄alkenyl and phenyl.
14. The process according to any one of claims 1-13, wherein the groups R⁷ to R¹⁰ and R in the ligands of Formula III are unsubstituted.
15. The process according to any one of claims 1-14, wherein the aminodiphosphine ligand (P₂NH) of formula (III) is chiral.
16. The process according to any one of claims 1-15, wherein the ligand (P₂NH) is selected from one of the formulae III(a) – III(i) below:





wherein R^{12} simultaneously or independently are selected from the group consisting of halo, OH, NH_2 , OR^c , NR^c_2 and R^c in which R^c is selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl and aryl.

17. The process according to claim 16, wherein P2NH is a compound of formula III(a) and R^{12} is R^c , in which R^c is selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl and phenyl.

18. The process according to claim 17, wherein P2NH is a compound of formula III(a) and R^{12} is R^c , in which R^c is selected from the group consisting of C_{1-4} alkyl and phenyl.

19. The process according to claim 18, wherein P2NH is a compound of formula III(a) and R^{12} is R^c , in which R^c is selected from the group consisting of i-propyl and phenyl.

20. The process according to any one of claims 1-19, wherein the metal complex is prepared and isolated prior to its use in the process or the metal complexes is prepared in situ, in the hydrogenation medium, without isolation or purification, just before its use.

21. The process according to any one of claims 1-20, wherein the base in the transfer hydrogenation reaction, if used, is an organic non-coordinating base, an alkaline or alkaline-earth metal carbonate, a carboxylate salt or an alcoholate or hydroxide salt.

22. The process according to claim 21, wherein the base is an alcoholate or an hydroxide salt selected from the group consisting of compounds of formula $(R^{14}O)_2M'$ and $R^{14}OM''$, in which M' is an alkaline-earth metal, M'' is an alkaline metal and R^{14} is hydrogen or C_{1-6} alkyl.
- 5 23. The process according to any one of claims 1-22, wherein primary and secondary alcohols are employed as the hydrogen donor.
24. The process according to 23, wherein 2-propanol or 2-butanol is used as the hydrogen donor.
- 10 25. The process according to any one of claims 1-22, wherein carboxylic acids or their esters, are employed as the hydrogen donor.
26. The process according to claim 25, wherein at least some of the carboxylic acid is present
15 as an amine salt or ammonium salt.
27. The process according to claim 26, wherein the amine salt or ammonium salt is a tertiary amine.
- 20 28. The process according to claim 29, wherein the tertiary amine is a trialkyl amine.
29. The process according to claim 27, wherein the trialkyl amine is triethylamine.
30. The process according to any one of claims 26-29, wherein formic acid or
25 triethylammonium formate is used as the hydrogen donor.
31. The process according to any one of claims 1-30, wherein the transfer hydrogenation is carried out in the presence of a solvent.
- 30 32. The process according to claim 31, wherein the transfer hydrogenation is carried out in a primary or secondary alcohol as the solvent.

33. The process according to claim 31, wherein the solvent is selected from benzene, toluene, xylene, hexane, cyclohexane, tetrahydrofuran, and primary or secondary alcohols, and mixtures thereof.

5 34. The process according to 31, wherein the solvent is a primary, secondary or tertiary amine.

35. The process according to any one of claims 1-34, wherein the transfer hydrogenation reaction is carried out in the presence of hydrogen gas.

10

36. The process according to any one of claims 1-34, wherein the transfer hydrogenation procedure is carried out in the presence of an inert gas or in the presence of air.

37. The process according to claim 36, wherein the inert gas is nitrogen or argon.

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FIGURE 1

