PHOSPHORUS COMPOUNDS AND METHODS THEREOF

Technical Field

The present invention relates, in general terms, to phosphorus compounds and methods of synthesising these compounds.

Background

Tetramethylpiperidine has been known for over a century, yet surprisingly its phosphine analogues (for example, 2,2,6,6-tetramethylphosphinane; **TMP**) are not as commonly used. Further, while some of the phosphorus compounds such as TMP are known, there is no known synthesis. The amine version (2,2,6,6-tetramethylpiperidine) has widespread application as a base, and nitrogen heterocycle in organic chemistry. Closely related to TMP is di-tert-butylphosphine, a specialty phosphine synthon equivalent, again having widespread application in organic chemistry as well as several commercial phosphine ligands, including: JohnPhos (cross-coupling chemistry) as well as DTBPX (Mitsubishi-Lucite Alpha Process).

The synthesis of organophosphorus compounds often requires the use of highly reactive (toxic) precursors such as phosphine gas (PH_3) or phosphorus trichloride (PCl_3). For example, di-*tert*-butylphosphine can be obtained from the reduction of di-*tert*-butylchlorophosphine which is itself obtained from phosphorus trichloride and the corresponding Grignard reagent.

Di-*tert*-butylchlorophosphine and phosphorus trichloride are a skin irritant and toxic when inhaled. As such, given the hazardous nature of phosphorus precursors and the need to enforce health and safety measures on an industrial level, a pragmatic approach taken is often to use a non-phosphine alternative which is generally safer to handle.

Current methodology for introducing a TMP synthon in a molecule involves incorporating the phosphorus early as R-PH_2 which is then subsequently condensed with phorone. This results in a low yield and potentially high impurity content.

Further, current methods for synthesising phosphorus compounds are lengthy (many

reaction steps) and are also not suitable for synthesising bulky phosphorus heterocycles; i.e. low yields are reported.

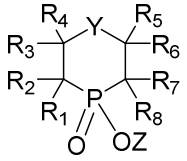
It is desirable to develop synthetic routes from more benign air stable phosphorus precursors.

It would be desirable to overcome or ameliorate at least one of the above-described problems.

Summary

The present invention is predicated on the understanding that there are a number of primary phosphine surrogates that can be generated *in situ* from less reactive, air-stable precursors. One example is bis(trimethylsilyl) phosphonite which can be derived from derivatives of commercially available and relatively benign hypophosphorous acid or its salts.

The present invention provides a method of synthesising a phosphorus compound of Formula (I), a salt, solvate or isomer thereof:



(I)

wherein Y is selected from an optionally substituted C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene, optionally substituted silylene, optionally substituted aminoylene, acylene, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^{+}(R_9R_{10})-$;

Z is selected from H, optionally substituted alkyl or a metal cation;

R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;

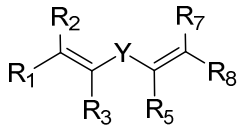
R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted

alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl;

the method comprising:

a) reacting a compound of Formula (A) with a hypophosphite ester, acid, salt or solvate thereof and an optional organosilicon compound, the compound of Formula (A) is



(A)

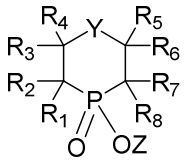
wherein Y is selected from an optionally substituted $C_{1\text{-}10}$ alkylene, optionally substituted $C_{1\text{-}10}$ alkenylene, optionally substituted silylene, optionally substituted amino, acylene, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^{+}(R_{13}R_{14})-$;

wherein R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

wherein R_1 and R_8 can be linked to form an optionally substituted cyclo moiety;

R_3 and R_5 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl.

Disclosed herein is method of synthesising a phosphorus compound of Formula (I), a salt, solvate or stereoisomer thereof:



(I)

wherein Y is selected from an optionally substituted C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene, optionally substituted silylene, optionally substituted aminoylene, acylene, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^{+}(R_9R_{10})-$;

Z is selected from H, optionally substituted alkyl or a metal cation;

R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

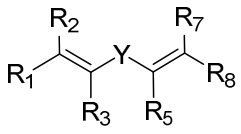
wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;

R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl;

the method comprising:

a) reacting a compound of Formula (A) with a hypophosphite ester, acid, salt or solvate thereof and an organosilicon compound, the compound of Formula (A) is



(A)

wherein Y is selected from an optionally substituted C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene, optionally substituted silylene, optionally substituted amino, acylene, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^{+}(R_9R_{10})-$;

wherein R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl;

optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

wherein R_1 and R_8 can be linked to form an optionally substituted cyclo moiety;

R_3 and R_5 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl.

In some embodiments, the hypophosphite ester, acid, salt or solvate thereof is selected from hypophosphorous acid (H_3PO_2), ammonium hypophosphite ($NH_4H_2PO_2$) and sodium hypophosphite ($NaPO_2H_2$), potassium hypophosphite, calcium bis(hypophosphite), copper hypophosphite, nickel(II) bis(hypophosphite), magnesium hypophosphite, anilinium hypophosphite, methyl hypophosphite, ethyl hypophosphite, or a combination thereof.

In some embodiments, the organosilicon compound is selected from bis(trimethylsilyl)amine (HMDS), *N,N*-Bis(trimethylsilyl)methylamine, bis(dimethylamino)dimethylsilane, N,O-bis(trimethylsilyl)acetamide (BSA), N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA), *N,N*-dimethyltrimethylsilylamine, hexamethyldisiloxane, *N,N*-diethyltrimethylsilylamine 1-(trimethylsilyl)pyrrolidine trimethylsilyl chloride (TMSCl), trimethylsilyl bromide (TMSBr), chlorotriethylsilane, and a combination thereof.

Further advantageously, these phosphorus compounds, and in particular ammonium hypophosphite, are stable in air.

In some embodiments, a molar ratio of hypophosphite ester, acid, salt or solvate thereof to the organosilicon compound is about 1:10 to about 1:1.

In some embodiments, the step of reacting a compound of Formula (A) with the hypophosphite ester, acid, salt or solvate thereof and the organosilicon compound

further comprises a base.

In some embodiments, the base is selected from triethylamine, diethylamine, Hünigs base, pyrrolidine, pyridine, lutidine, piperidine 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,4-diazabicyclo[2.2.2]octane (DABCO), sodium hydroxide, potassium hydroxide, ammonium hydroxide, sodium carbonate, sodium hydrogen carbonate, barium hydroxide, calcium carbonate, caesium carbonate, or a combination thereof.

In some embodiments, the step of reacting a compound of Formula (A) with the hypophosphite ester, acid, salt or solvate thereof and the organosilicon compound further comprises a solvent.

In some embodiments, the solvent is selected from tetrahydrofuran (THF), toluene, xylenes, methylene chloride, dichloroethane, tetrachloroethane, ethers, dimethylacetamide (DMA), or a combination thereof.

In some embodiments, the method further comprises a step of treating a product of step (a) with an acid.

In some embodiments, the compound of Formula (A) is reacted with the hypophosphite ester, acid, salt or solvate thereof and the organosilicon compound at a temperature of about 70 °C to about 150 °C.

Further advantageously, the higher temperature promotes the ring closure reaction such that a bulky heterocyclyl compound of formula (I) can be formed.

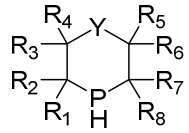
In some embodiments, the method further comprises a step (b) after (a) of modifying the compound of formula (I) at the Y moiety.

In some embodiments, the method further comprises a step (b) after (a) of modifying the compound of formula (I) with a protecting group compound.

In some embodiments, the protecting group compound is selected from ethylene glycol, methanol, ethanol, propylene glycol, 2,2-dimethyl-1,3-propanediol (neopentylglycol), dimethyl hydrazine, 1,2-ethanedithiol and 1,3-propanedithiol.

In some embodiments, the method further comprises a step of reducing the compound of formula (I). This reduction step can take place after step (a) or after the modification step (b).

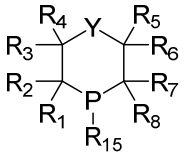
In some embodiments, the method further comprises a step reducing the phosphorus compound of Formula (I) in order to form a phosphorus compound of Formula (II):



(II)

wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and Y are as disclosed herein.

In some embodiments, the method further comprises of functionalising the compound of Formula (II) in order to form a phosphorus compound of Formula (III):



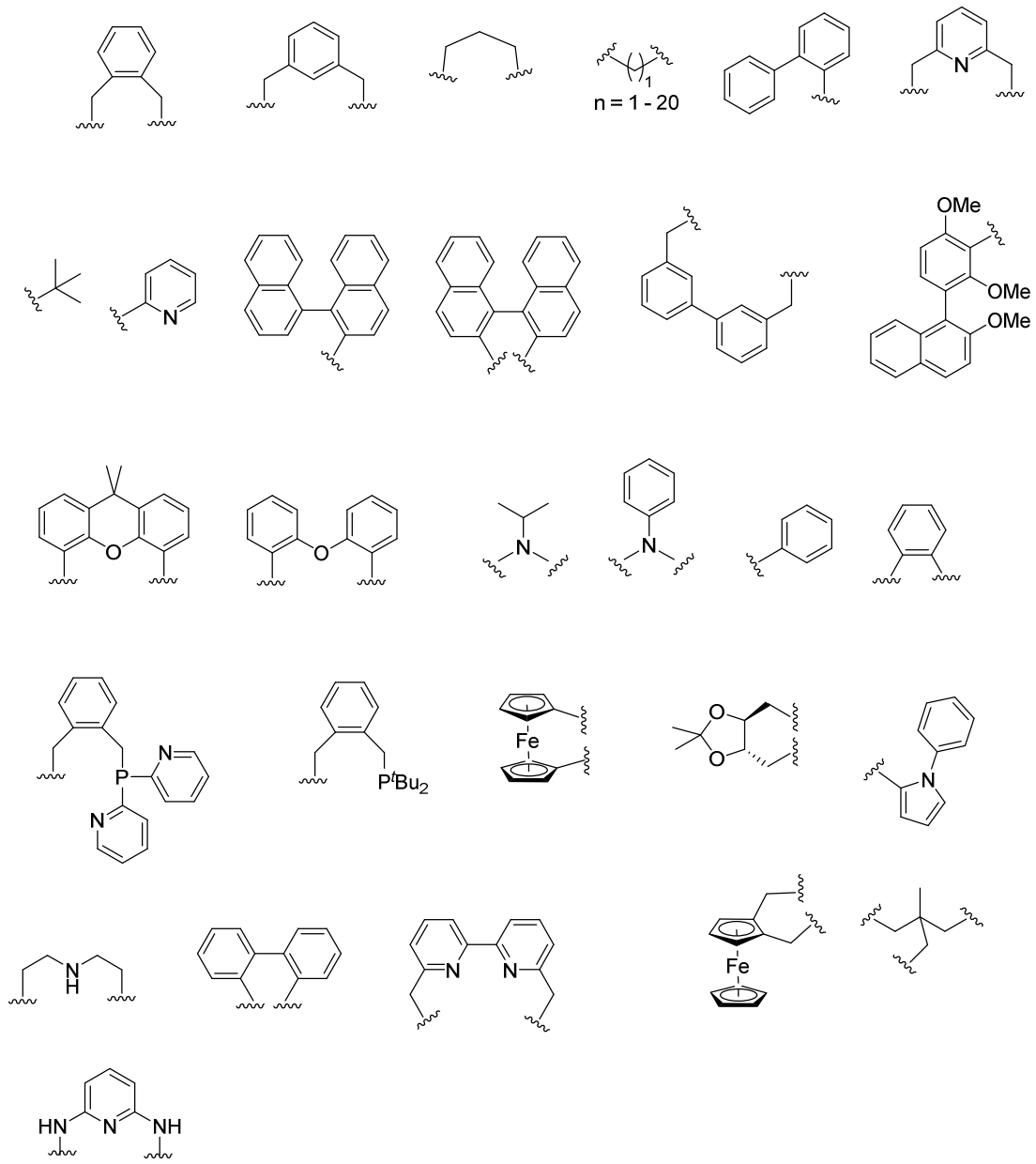
(III)

wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and Y are as disclosed herein;

R_{15} is selected from halo, oxo, optionally substituted amino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl.

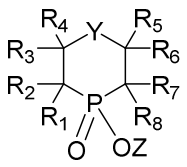
In some embodiments, the optional substituent at R_{15} comprises another compound of Formula (III).

In some embodiments, the optional substituent at R_{15} is selected from:



wherein ~ represents a bond to R_{15} of compound of Formula (III).

The present invention also provides a phosphorus compound of Formula (I), a salt, solvate or isomer thereof:



(I)

wherein Y is selected from an optionally substituted C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene, optionally substituted silylene, optionally substituted amino, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^{+}(R_9R_{10})-$;

Z is selected from H, optionally substituted alkyl or a metal cation;

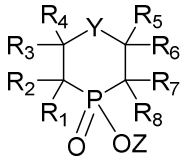
R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;

R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl; and

R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl.

Disclosed herein is a phosphorus compound of Formula (I), a salt, solvate or stereoisomer thereof:



(I)

wherein Y is selected from an optionally substituted C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene, optionally substituted silylene, optionally substituted amino, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^{+}(R_9R_{10})-$;

Z is selected from H, optionally substituted alkyl or a metal cation;

R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl,

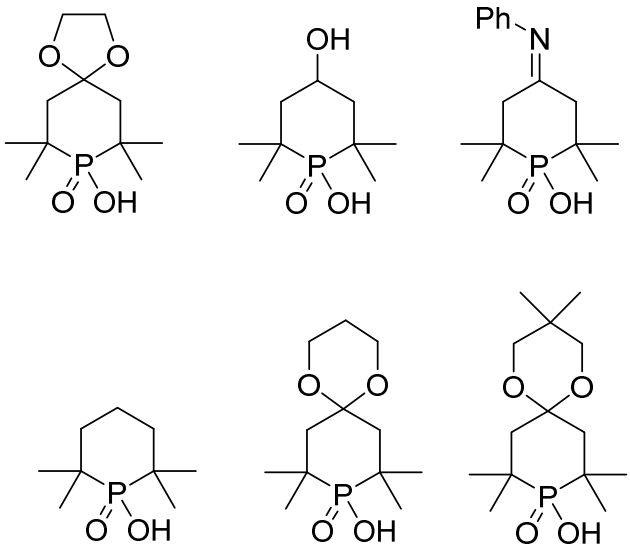
optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

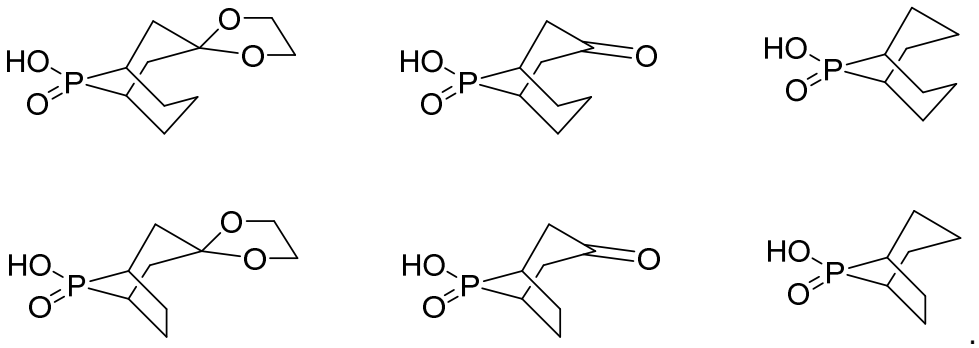
wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;

R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl; and

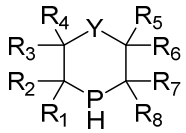
R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl.

In some embodiments, the compound of Formula (I) is selected from:





The present invention also provides a phosphorus compound of Formula (II), a salt, solvate or isomer thereof:



(II)

wherein Y is selected from an optionally substituted C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene,, optionally substituted silylene, optionally substituted amino, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^{+}(R_9R_{10})-$;

R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally

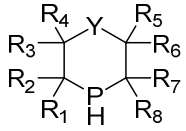
substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;

R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl.

Disclosed herein is a phosphorus compound of Formula (II), a salt, solvate or stereoisomer thereof:



(II)

wherein Y is selected from an C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene, optionally substituted silylene, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or -$P^+(R_9R_{10})$-;

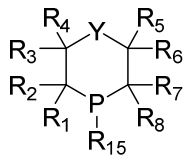
R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;

R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl.

The present invention also provides a phosphorus compound of Formula (III), a salt, solvate or isomer thereof:



(III)

wherein Y is selected from an optionally substituted C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene, optionally substituted silylene, optionally substituted amino, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^+(R_9R_{10})-$;

R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;

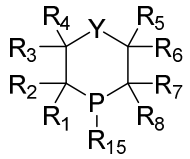
R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl; and

R_{15} is selected from halo, oxo, optionally substituted amino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl.

Disclosed herein is a phosphorus compound of Formula (III), a salt, solvate or

stereoisomer thereof:



(III)

wherein Y is selected from an C_{1-10} alkylene optionally substituted with acyl or 1,2-ethanedioxy or 1,3-propanedioxy or 2,2-dimethyl-1,3-propanedioxy, optionally substituted C_{1-10} alkenylene, optionally substituted silylene, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^{+}(R_9R_{10})-$;

R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;

R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl; and

R_{15} is selected from halo, oxo, optionally substituted amino, alkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, optionally substituted m-xylenyl, optionally substituted pyridinylmethyl, optionally substituted biphenylmethyl, 2-(compound of Formula (III))biphenyl, optionally substituted binaphthyl, optionally substituted phenylnaphthyl, optionally substituted diphenyl oxide, and another compound of Formula (III).

Detailed description

Current methods of synthesising secondary phosphorus compounds of type (II) are rare. For example, a lithium cleavage of a P-phenyl bond had previously been proposed. However, in this example, the lithium cleavage of phenylphosphorinone is both atomically uneconomical (generating lots of waste) and unselective, due to the preference of the lithium cleavage to occur at the P-alkyl bond instead of the P-aryl bond, giving yields of only 27%.

The present invention is based on the understanding that bis(trimethylsilyl) phosphonite can react with primary alkyl halides to give alkyl substituted primary and secondary phosphinic acids. Bis(trimethylsilyl) phosphonite can also react with one equivalent of an α,β-unsaturated ketone to furnish primary phosphinic acids, or two equivalents of an α,β-unsaturated ketone to furnish secondary phosphinic acids.

The present invention utilises a group linking together two Michael acceptor groups e.g. such as dienones to react with a silylphosphonite to access phosphorus heterocycles. In particular, the consecutive reaction at two geminally substituted alkenes to give a high yield of final product. It was further found that the silylphosphonite can be generated in situ in the presence of a phosphorus precursor, such as ammonium hypophosphite, and a silyl precursor.

In addition, and advantageously, the present invention enables reaction at sterically hindered disubstituted alkenes. When compared with previous synthetic reactions, because of the additional steric hindrance of geminally di-substituted alkenes, the previous reactions are sluggish, and give products with low yields or no reaction whatsoever. For example, the hydrophosphination of alkenes does not generally occur at geminally disubstituted alkenes, often resulting in no reaction. Further advantageously, a bulky cyclyl phosphorus compound can be synthesised with two equivalents of an α,β-unsaturated ketone which are at least di-substituted on both alkenes. In particular, the second addition of an α,β-unsaturated ketone containing the substituted alkene can progress smoothly to give a product with good yield.

Heterocyclic phosphorus compounds possess unique properties and have increasing applications, for example as ligands. It would therefore be desirable to have a method which both tolerates substituted α,β-unsaturated ketones and leads to the formation of heterocyclic phosphinic acids. The use of dienones as an alternative substrate and the

application of specific reaction conditions is believed to enable the practical synthesis of heterocyclic phosphinic acids in this manner. By providing a phosphorus synthon equivalent that is readily modifiable, a convergent synthetic approach can be taken to streamline the number of reactions required in the synthesis.

In some embodiments, heterocyclic secondary phosphinic acid 2,2,6,6-tetramethylphosphorinic acid (P1), derivatives (P2, P3, TMP, ATMP and KTMP) and methods to synthesise them are disclosed. Reduction of the phosphinic acid groups generates secondary phosphines which can be readily transformed into useful phosphine ligands by reaction of the P-H ligand to generate tertiary phosphines.

"Alkyl" refers to monovalent alkyl groups which may be straight chained or branched and preferably have from 1 to 10 carbon atoms or more preferably 1 to 6 carbon atoms. Examples of such alkyl groups include methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *iso*-butyl, *n*-hexyl, and the like.

"Alkylene" refers to divalent alkyl groups preferably having from 1 to 10 carbon atoms and more preferably 1 to 6 carbon atoms. Examples of such alkylene groups include methylene (-CH_2-), ethylene (-CH_2CH_2-), and the propylene isomers (e.g., -$CH_2CH_2CH_2$- and –$CH(CH_3)CH_2$-), and the like.

"Alkenyl" refers to a monovalent alkenyl group which may be straight chained or branched and preferably have from 2 to 10 carbon atoms and more preferably 2 to 6 carbon atoms and have at least 1 and preferably from 1-2, carbon to carbon, double bonds. Examples include ethenyl (-$CH=CH_2$), *n*-propenyl (-$CH_2CH=CH_2$), *iso*-propenyl (-$C(CH_3)=CH_2$), but-2-enyl (-$CH_2CH=CHCH_3$), and the like.

"Alkenylene" refers to divalent alkenyl groups preferably having from 2 to 8 carbon atoms and more preferably 2 to 6 carbon atoms. Examples include ethenylene (-CH=CH-), and the propenylene isomers (e.g., -$CH_2CH=CH$- and –$C(CH_3)=CH$-), and the like.

"Alkynyl" refers to alkynyl groups preferably having from 2 to 10 carbon atoms and more preferably 2 to 6 carbon atoms and having at least 1, and preferably from 1-2, carbon to carbon, triple bonds. Examples of alkynyl groups include ethynyl (-C≡ CH),

propargyl (-$CH_2C\equiv$ CH), pent-2-ynyl (-$CH_2C\equiv CCH_2$-CH_3), and the like.

"Alkynylene" refers to the divalent alkynyl groups preferably having from 2 to 8 carbon atoms and more preferably 2 to 6 carbon atoms. Examples include ethynylene (-C≡ C-), propynylene (-CH_2-C≡ C-), and the like.

"Alkoxy" refers to the group alkyl-O- where the alkyl group is as described above. Examples include, methoxy, ethoxy, *n*-propoxy, *iso*-propoxy, *n*-butoxy, *tert*-butoxy, *sec*-butoxy, *n*-pentoxy, *n*-hexoxy, 1,2-dimethylbutoxy, and the like.

"Halo" or "halogen" refers to fluoro, chloro, bromo and iodo.

"Oxo/hydroxy" refers to groups =O, HO-.

"Alkoxy" refers to the group alkyl-O- where the alkyl group is as described above. Examples include, methoxy, ethoxy, *n*-propoxy, *iso*-propoxy, *n*-butoxy, *tert*-butoxy, *sec*-butoxy, *n*-pentoxy, *n*-hexoxy, 1,2-dimethylbutoxy, and the like.

"Amino" refers to the group –NR"R" where each R" is independently hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl and where each of alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl is as described herein.

"Aminoylene" refers to the group –N(R")- where R" is hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl and where each of alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl is as described herein.

"Aryl" refers to an unsaturated aromatic carbocyclic group having a single ring (eg. phenyl) or multiple condensed rings (eg. naphthyl or anthryl), preferably having from 6 to 14 carbon atoms. Examples of aryl groups include phenyl, naphthyl and the like.

"Heteroaryl" refers to a monovalent aromatic heterocyclic group which fulfils the Hückel criteria for aromaticity (ie. contains 4n + 2 π electrons) and preferably has from 2 to 10 carbon atoms and 1 to 4 heteroatoms selected from oxygen, nitrogen, selenium, and sulfur within the ring (and includes oxides of sulfur, selenium and

nitrogen). Such heteroaryl groups can have a single ring (eg. pyridyl, pyrrolyl or N-oxides thereof or furyl) or multiple condensed rings (eg. indolizinyl, benzoimidazolyl, coumarinyl, quinolinyl, isoquinolinyl or benzothienyl).

Examples of heteroaryl groups include, but are not limited to, oxazole, pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, indolizine, isoindole, indole, indazole, purine, isoquinoline, quinoline, phthalazine, naphthylpyridine, quinoxaline, quinazoline, cinnoline, pteridine, carbazole, carboline, phenanthridine, acridine, phenanthroline, isothiazole, phenazine, isoxazole, isothiazole, phenoxazine, phenothiazine, thiazole, thiadiazoles, oxadiazole, oxatriazole, tetrazole, thiophene, benzo[b]thiophene, triazole, imidazopyridine and the like.

"Acyl" refers to groups H-C(O)-, alkyl-C(O)-, cycloalkyl-C(O)-, aryl-C(O)-, heteroaryl-C(O)- and heterocyclyl-C(O)-, where alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl are as described herein.

"Acylene" refers to the divalent acyl group; i.e. –C(O)-.

"Cycloalkyl" refers to cyclic alkyl groups having a single cyclic ring or multiple condensed rings, preferably incorporating 3 to 11 carbon atoms. Such cycloalkyl groups include, by way of example, single ring structures such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclooctyl, and the like, or multiple ring structures such as adamantanyl, indanyl, 1,2,3,4-tetrahydronapthalenyl and the like.

"Cycloalkenyl" refers to cyclic alkenyl groups having a single cyclic ring or multiple condensed rings, and at least one point of internal unsaturation, preferably incorporating 4 to 11 carbon atoms. Examples of suitable cycloalkenyl groups include, for instance, cyclobut-2-enyl, cyclopent-3-enyl, cyclohex-4-enyl, cyclooct-3-enyl, indenyl and the like.

"Heterocyclyl" refers to a monovalent saturated or unsaturated group having a single ring or multiple condensed rings, preferably from 1 to 8 carbon atoms and from 1 to 4 hetero atoms selected from nitrogen, sulfur, oxygen, selenium or phosphorous within the ring. The most preferred heteroatom is nitrogen. It will be understood

that where, for instance, R_2 or R' is an optionally substituted heterocyclyl which has one or more ring heteroatoms, the heterocyclyl group can be connected to the core molecule of the compounds of the present invention, through a C-C or C-heteroatom bond, in particular a C-N bond.

Examples of heterocyclyl and heteroaryl groups include, but are not limited to, oxazole, pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, indolizine, isoindole, indole, indazole, purine, quinolizine, isoquinoline, quinoline, phthalazine, naphthylpyridine, quinoxaline, quinazoline, cinnoline, pteridine, carbazole, carboline, phenanthridine, acridine, phenanthroline, isothiazole, phenazine, isoxazole, isothiazole, phenoxazine, phenothiazine, imidazolidine, imidazoline, piperidine, piperazine, indoline, phthalimide, 1,2,3,4-tetrahydroisoquinoline, 4,5,6,7-tetrahydrobenzo[b]thiophene, thiazole, thiadiazoles, oxadiazole, oxatriazole, tetrazole, thiazolidine, thiophene, benzo[b]thiophene, morpholino, piperidinyl, pyrrolidine, tetrahydrofuranyl, triazole, and the like.

"Thio" refers to groups H-S-, alkyl-S-, cycloalkyl-S-, aryl-S-, heteroaryl-S-, and heterocyclyl-S-, where alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl are as described herein.

"Thioacyl" refers to groups H-C(S)-, alkyl-C(S)-, cycloalkyl-C(S)-, aryl-C(S)-, heteroaryl-C(S)-, and heterocyclyl-C(S)-, where alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl are as described herein.

"Thioacylene" refers to the divalent thioacyl group; i.e. -C(S)-.

"Sulfinyl" refers to groups H-S(O)-, alkyl-S(O)-, cycloalkyl-S(O)-, aryl-S(O)-, heteroaryl-S(O)-, and heterocyclyl-S(O)-, where alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl are as described herein.

"Sulfinylene" refers to the divalent sulfinyl group; i.e. -S(O)-.

"Sulfonyl" refers to groups H-$S(O)_2$-, alkyl-$S(O)_2$-, cycloalkyl-$S(O)_2$-, aryl-$S(O)_2$-, heteroaryl-$S(O)_2$-, and heterocyclyl-$S(O)_2$-, where alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl are as described herein.

"Sulfonylene" refers to the divalent sulfonyl group; i.e. -$S(O)_2$-.

"Silyl" refers to groups which contain a covalently bonded silicon atom, and include groups $-Si(R")_3$, $-Si(OR")(R")(R")$, $-Si(OR")_2(R")$, $-Si(OR")_3$ where R" is independently hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl and where each of alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl is as described herein.

"Silylene" refers to divalent silyl groups; $-Si(R")_2$-, $-Si(OR")(R")$-, $-Si(OR")_2$-, where R" is independently hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, and heterocyclyl and where each of alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl is as described herein.

In this specification "optionally substituted" is taken to mean that a group may or may not be further substituted or fused (so as to form a condensed polycyclic group) with one or more groups selected from hydroxyl, acyl, alkyl, alkoxy, alkenyl, alkenyloxy, alkynyl, alkynyloxy, amino, aminoacyl, thio, arylalkyl, arylalkoxy, aryl, aryloxy, carboxyl, acylamino, cyano, halogen, nitro, phosphono, sulfo, phosphorylamino, phosphinyl, heteroaryl, heteroarylalkyl, heteroaryloxy, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, oxyacyl, oxime, oxime ether, hydrazone, oxyacylamino, oxysulfonylamino, aminoacyloxy, trihalomethyl, trialkylsilyl, pentafluoroethyl, trifluoromethoxy, difluoromethoxy, trifluoromethanethio, trifluoroethenyl, mono- and di-alkylamino, mono-and di-(substituted alkyl)amino, mono- and di-arylamino, mono- and di-heteroarylamino, mono- and di-heterocyclyl amino, and unsymmetric di-substituted amines having different substituents selected from alkyl, aryl, heteroaryl and heterocyclyl, and the like, and may also include a bond to a solid support material, (for example, substituted onto a polymer resin). For instance, an "optionally substituted amino" group may include amino acid and peptide residues.

"Phosphoryl" refers to the groups -P(O)(R''')(OR'''') where R'' represents H, alkyl, cycloalkyl, alkenyl, or aryl, R''' represents OR'''' or is hydroxy or amino and R'''' is alkyl, cycloalkyl, aryl or arylalkyl, where alkyl, amino, alkenyl, aryl, cycloalkyl, and arylalkyl are as described herein.

"Phosphonate" refers to an organophosphorus compound containing a $-PO(OR)_2$, where the phosphorus atom is linked to a carbon, and where R can independently represent H, alkyl, cycloalkyl, alkenyl, aryl, arylalkyl, heteroarylalkyl or heteroaryl as described herein.

"Phosphonite" refers to an organophosphorus compound with the formula $P(OR)_2R$, where R can independently represent H, alkyl, cycloalkyl, alkenyl, aryl, arylalkyl, heteroarylalkyl or heteroaryl as described herein.

"Phosphinite" refers to an organophosphorus compound with the formula $P(OR)R_2$, where R can independently represent H, alkyl, cycloalkyl, alkenyl, aryl, arylalkyl, heteroarylalkyl or heteroaryl as described herein.

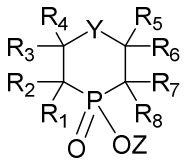
"Phosphinate" or "hypophosphite" refers to phosphorus compounds with the formula $PO(OR)R_2$, where R can independently represent H, alkyl, cycloalkyl, alkenyl, aryl, arylalkyl, heteroarylalkyl or heteroaryl as described herein. "Phosphinic acid" refers to a phosphorus oxyacid with the formula $PO(OH)R_2$.

"Phosphine" refers to phosphorus compounds with the formula PR_3, where R can independently represent H, alkyl, cycloalkyl, alkenyl, aryl, arylalkyl, heteroarylalkyl or heteroaryl as described herein. For example, a primary hydrocarbylphosphine has a formula PH_2R, where R can be alkyl, cycloalkyl or arylalkyl.

"Solvent" as used herein, refers to an organic based solvent or solvent system, and which comprises of mainly organic solvent. Organic based solvents can be any carbon based solvents. Such solvents can be either polar or non-polar, and/or either protic or aprotic. Solvent systems refer to combinations of solvents which resulting in a final single phase. Both 'solvents' and 'solvent systems' can include, and is not limited to, pentane, cyclopentane, hexane, cyclohexane, benzene, toluene, dioxane, chloroform, diethylether, dichloromethane, tetrahydrofuran, ethyl acetate, acetone, dimethylformamide, acetonitrile, dimethyl sulfoxide, nitromethane, propylene carbonate, formic acid, butanol, isopropanol, propanol, ethanol, methanol, acetic acid, ethylene glycol, diethylene glycol or water. Organic based solvents or solvent systems can include, but not limited to, any non-polar liquid which can be hydrophobic and/or

lipophilic. As such, oils such as animal oil, vegetable oil, petrochemical oil, and other synthetic oils are also included within this definition.

The present invention provides a method of synthesising a phosphorus compound of Formula (I), a salt, solvate or isomer thereof:



(I)

wherein Y is selected from an optionally substituted C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene, optionally substituted silylene, optionally substituted amino, acylene, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^{+}(R^{9}R^{10})-$;

Z is selected from H, optionally substituted alkyl or a metal cation;

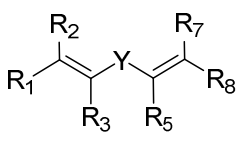
R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

R^9 and R^{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl;

the method comprising:

a) reacting a compound of Formula (A) with a hypophosphite ester, acid, salt or solvate thereof and an optional organosilicon compound, the compound of Formula (A) is



(A)

wherein Y is selected from an optionally substituted C_{1-10} alkylene, optionally substituted C_{1-10} alkylenylene,, optionally substituted silicon, acylene, -C(OR^9)(OR^{10})-, -C(OCH$_2$CH$_2$O)-, -C(OCH$_2$CH$_2$CH$_2$O)-, -C(=NR^{11})-, -CH(NR^{11}R^{12})-, -N(R^{11})-, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or -P$^+$(R^{13}R^{14})-;

wherein R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

R_3 and R_5 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl; and

wherein R_1 and R_8 can be linked to form an optionally substituted cyclo moiety.

The organosilicon compound acts to protect the oxygen atom covalently bonded to the phosphorus atom. Accordingly, the organosilicon compound can be optional if, for example, a hypophosphite ester is used; i.e. the oxygen atom is already in a protected form and so may not require silylation. The silylated hypophosphite is believed to be more reactive. Due to silyl migration, the other alkene bond in compound of Formula (A) is no longer a good Michael acceptor (it is not in the enone form) and can be purified as an intermediate (for example compound of Formula (Aii); see below). The compound of Formula (Aii) can be silyated again to give the final product. By splitting up the steps, a better yield is obtainable. On the other hand, a hypophosphite ester is less reactive in the Michael addition, but may be able to add twice consecutively and thus form the final product in a single step.

The hypophosphite ester, acid, salt or solvate thereof and the organosilicon compound reacts to form a silylphosphorus precursor. The compound of Formula (A) reacts with the silylphosphorus precursor in that the phosphorus atom is added to the alkene carbon of the compound of Formula (A) which is more substituted.

In some embodiments, Y is selected from optionally substituted C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene, optionally substituted silylene, acylene, -N(R_{13})-, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or -P^+(R_9R_{10})-. In other embodiments, Y is selected from optionally substituted C_{1-5} alkylene, optionally substituted silylene, acylene, -N(R_{13})-, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or -P^+(R_9R_{10})-. In other embodiments, Y is selected from optionally substituted C_{1-4} alkylene, acylene, -N(R_{13})-, thioacylene, sulfinylene, sulfonylene, or -P(O)(OZ)-.

In some embodiments, Y is optionally substituted with oxo, halo, optionally substituted alkyl; optionally substituted haloalkyl, optionally substituted oxyalkyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl. In other embodiments, Y is optionally substituted with oxo, halo, optionally substituted C_1-C_6 alkyl; optionally substituted C_1-C_6 haloalkyl, optionally substituted C_1-C_6 oxyalkyl, optionally substituted C_4-C_{12} cycloalkyl, optionally substituted C_4-C_{12} heterocyclyl, optionally substituted C_4-C_{12} heteroaryl, and optionally substituted C_4-C_{12} aryl.

In some embodiments, Y is optionally substituted with alkyl, alkoxy, cycloalkyl, heterocyclyl, or oxo. In other embodiments, the optional substituent is C_1-C_6 alkyl, -O or –OH.

In other embodiments, the optionally substituted C_{1-10} alkylene is optionally substituted with one or two alkoxy (acetal groups). When the optionally substituted C_{1-10} alkylene is optionally substituted with two alkoxy, the two alkoxy can be linked to form a heterocyclyl (cycloacetal). In this regard, a spiro moiety is formed at Y. The optionally substituted alkoxy can be -C(OR_{11})(OR_{12})-, wherein R_{11} and R_{12} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl. When the two alkoxy linked, the spiro moiety can for example be -C($OR_{11}R_{12}O$)-, -C(OCH_2CH_2O)- or -C($OCH_2CH_2CH_2O$)-. In other embodiments, the optionally substituted C_{1-10} alkylene is optionally substituted with amino. For example, optionally substituted C_{1-10} alkylene is -C(=NR_{13})- or -CH($NR_{13}R_{14}$)-, wherein R_{13} and R_{14} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl. In other embodiments, Y is dionylene.

In some embodiments, R_1, R_2, R_7 and R_8 are independently selected from optionally substituted C_1-C_6 alkyl; optionally substituted C_1-C_6 haloalkyl; optionally substituted C_1-C_6 oxyalkyl; optionally substituted C_4-C_{12} cycloalkyl, optionally substituted C_4-C_{12} heterocyclyl, optionally substituted C_4-C_{12} heteroaryl, and optionally substituted C_4-C_{12} aryl. In other embodiments, R_1, R_2, R_4 and R_5 are independently selected from optionally substituted C_1-C_6 alkyl; optionally substituted C_1-C_6 haloalkyl; optionally substituted C_1-C_6 oxyalkyl; optionally substituted C_4-C_{12} cycloalkyl, optionally substituted C_4-C_{12} heterocyclyl. In other embodiments, R_1, R_2, R_4 and R_5 are independently selected from C_1-C_6 alkyl. In other embodiments, R_1, R_2, R_4 and R_5 are independently selected from methyl, ethyl, n-propyl, iso-propyl, cyclopropyl, n-butyl, iso-butyl, sec-butyl, tert-butyl and cyclobutyl.

In some embodiments, R_1 and R_8 is linked to form an optionally substituted cyclo moiety. For example, R_1 and R_8 can be linked such that compound of Formula (A) is a cycloalkyl dienone, such as cycloheptadiene, cyclooctadiene, cyclononadiene, cycloheptadienone, cyclooctadienone and cyclononadienone. Accordingly, the resultant phosphorus compound can be a bicyclo-compound. In some embodiments, the phosphorus atom is a member of a bridge linkage. In other embodiments, the phosphorus atom is not a bridgehead atom. In other embodiments, the phosphorus atom is a member of the bicyclic skeletal structure.

In some embodiments, R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted alkyl, and optionally substituted haloalkyl. In other embodiments, R_3 and R_5 are independently H. In some embodiments, R_4 and R_6 are independently selected from H or optionally substituted alkyl. In other embodiments, R_4 and R_6 are independently selected from H, methyl, ethyl, or propyl.

In some embodiments, R^9, R^{10}, R^{11}, R^{12}, R^{13} and R^{14} are independently selected from H, optionally substituted C_1-C_{10} alkyl, optionally substituted C_3-C_{10} cycloalkyl, optionally substituted C_3-C_{10} heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl. In other embodiments, R^9, R^{10}, R^{11}, R^{12}, R^{13} and R^{14} are independently selected from H, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_3-C_{10} heterocycloyl, aryl, or heteroaryl. In other embodiments, R^9, R^{10}, R^{11}, R^{12}, R^{13} and R^{14} are independently selected from H, or C_1-C_5 alkyl.

In some embodiments, Z is selected from H, optionally substituted C_1-C_{10} alkyl or a metal cation. In some embodiments, Z is selected from H, C_1-C_5 alkyl or a metal cation. The metal cation can be Na^+, Li^+, or K^+.

In some embodiments, the organosilicon compound is selected from bis(trimethylsilyl)amine (HMDS), *N,N*-Bis(trimethylsilyl)methylamine, bis(dimethylamino)dimethylsilane, N,O-bis(trimethylsilyl)acetamide (BSA), N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA), *N,N*-dimethyltrimethylsilylamine, hexamethyldisiloxane, *N,N*-diethyltrimethylsilylamine 1-(trimethylsilyl)pyrrolidine trimethylsilyl chloride (TMSCl), trimethylsilyl bromide (TMSBr), chlorotriethylsilane, and a combination thereof. In some embodiments, the organosilicon compound is selected from bis(trimethylsilyl)amine (HMDS) and trimethylsilyl chloride (TMSCl).

In some embodiments, the hypophosphite ester, acid, salt or solvate thereof is selected from hypophosphorous acid (H_3PO_2), ammonium hypophosphite ($NH_4H_2PO_2$) and sodium hypophosphite ($NaPO_2H_2$), potassium hypophosphite, calcium bis(hypophosphite), copper hypophosphite, nickel(II) bis(hypophosphite), magnesium hypophosphite, anilinium hypophosphite, methyl hypophosphite, ethyl hypophosphite, or a combination thereof. In some embodiments, the hypophosphite ester, acid, salt or solvate thereof is selected from hypophosphorous acid (H_3PO_2) and ammonium hypophosphite ($NH_4H_2PO_2$). In other embodiments, the hypophosphite ester, acid, salt or solvate thereof is selected from hypophosphorous acid (H_3PO_2) or ammonium hypophosphite ($NH_4H_2PO_2$).

Further advantageously, these phosphorus compounds, and in particular ammonium hypophosphite, are stable in air.

As is discussed herein, the starting material passes through several intermediates to form the final product. In some embodiments, when organosilicon compound is used and to form a first intermediate (for example represented by Formula (Ai)), a molar ratio of hypophosphite ester, acid, salt or solvate thereof to the organosilicon compound is about 1:10, about 1:8, about 1:6, about 1:5, about 1:2, about 1:1.8, about 1:1.4, about 1:1.3, about 1:1.2, about 1:1.1 or about 2:10, about 3:10, about 4:10, about 5:10, about 6:10, or about 7:10. In other embodiments, the molar ratio is about 1:10

to about 1:1, about 2:10 to about 1:1, about 3:10 to about 1:1, about 4:10 to about 1:1, about 5:10 to about 1:1, about 6:10 to about 1:1, about 7:10 to about 1:1, about 8:10 to about 1:1, about 9:10 to about 1:1, or about 6:10 to about 8:10.

The organosilicon compound can be a bis(organosilicon) compound. In this regard, 2 Si moieties are available for reaction. In some embodiments, a ratio of the hypophosphite moiety to the organosilicon moiety is about 1:20 to about 1:1. In other embodiments, the ratio is about 1:18 to about 1:1, about 1:16 to about 1:1, about 1:14 to about 1:1, about 1:12 to about 1:1, about 1:10 to about 1:1, about 1:8 to about 1:1, about 1:6 to about 1:1, about 1:4 to about 1:1, or about 1:2 to about 1:1.

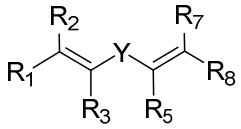
The hypophosphite ester, acid, salt or solvate thereof and the organosilicon compound can react to form a silylphosphorus precursor. In some embodiments, the silylphosphorus precursor is generated *in situ* from an organosilicon compound and hypophosphite ester, acid, salt or solvate thereof. The generation of a phosphine surrogate "in situ" is then reacted with a diene (for example, phorone) to furnish a compound of Formula (I).

In some embodiments, the step of reacting a compound of Formula (A) with the hypophosphite ester, acid, salt or solvate thereof and the organosilicon compound further comprises a base. For example, the base can be triethylamine, diethylamine, pyrrolidine, pyridine, lutidine, piperidine 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,4-diazabicyclo[2.2.2]octane (DABCO), sodium hydroxide, potassium hydroxide, ammonium hydroxide, sodium carbonate, sodium hydrogen carbonate, barium hydroxide, calcium carbonate, caesium carbonate, or a combination thereof. In other embodiments, the base is N,N-diisopropylethylamine. The base can be dependent on the organosilicon compound used. In some embodiments, a base is not required. For example, if HMDS is used, a base is not required. Where the organosilicon compound is trimethylsilyl chloride, Hünigs base can for example be used. In some embodiments, three equivalents of base to organosilicon compound is used.

In some embodiments, the step of reacting a compound of Formula (A) with the hypophosphite ester, acid, salt or solvate thereof and the organosilicon compound further comprises a solvent. In other embodiments, the solvent is a polar or nonpolar solvent. In general, a solvent can be selected to minimise intermolecular side reactions.

For example, depending on the reagents used, an aprotic solvent may be desirable as the reagents may react with a protic solvent e.g. an alcohol. In other embodiments, the solvent is selected from toluene, 1,2-dichloroethane, xylenes, chloroform, dichloromethane, diethylether, benzene, cyclohexane, hexane and pentane. In other embodiments, the solvent is selected from toluene, 1,2-dichloroethane, and xylenes.

In some embodiments, the compound of Formula (A) is

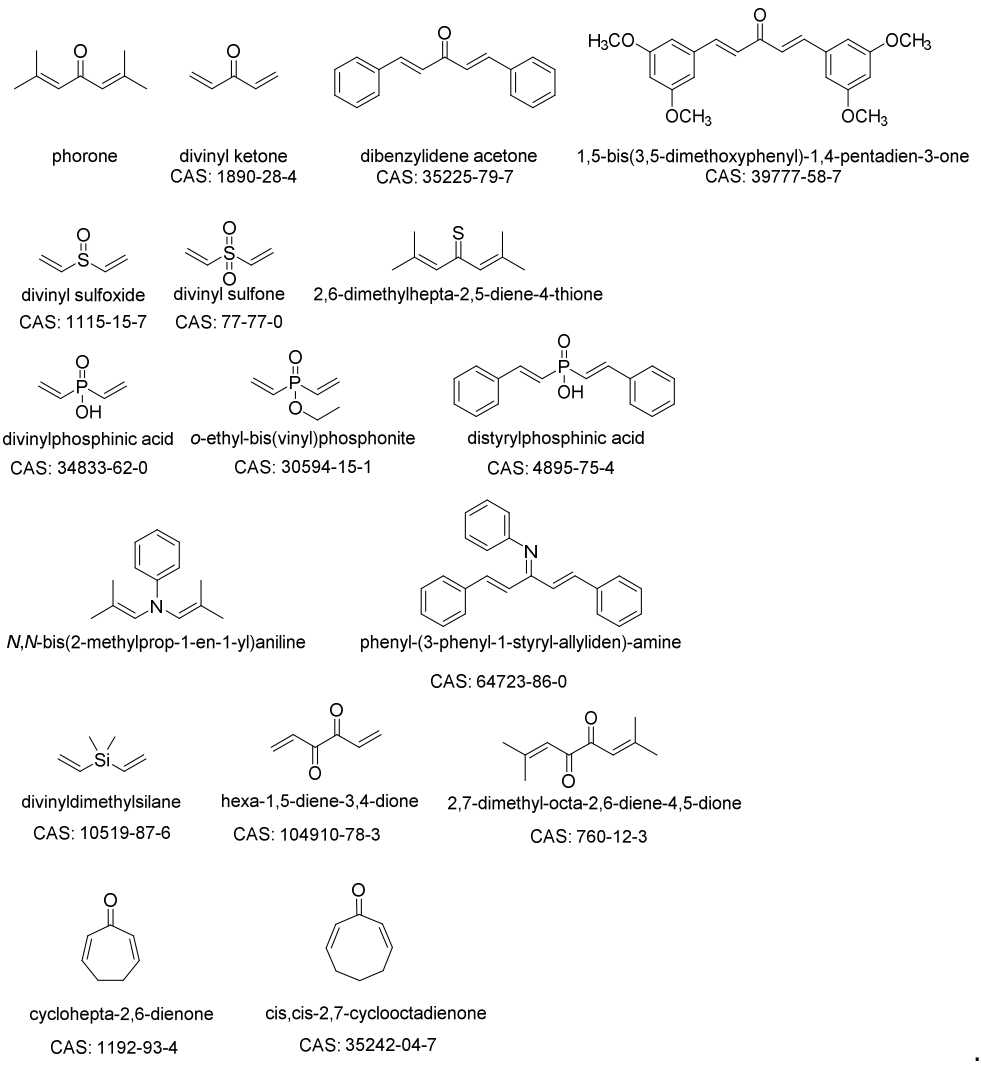


(A)

wherein R_1, R_2, R_3, R_5, R_7, R_8 and Y are as disclosed herein.

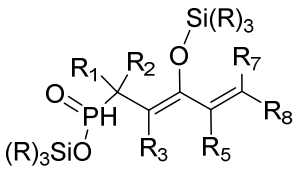
Some examples of compound of Formula (A) are divinyl ketone, dibenzylidene acetone, 1,5-bis(3,5-dimethoxyphenyl)1,4-pentadien-3-one, divinyl sulfoxide, divinyl sulfone, 2,6-dimethylhepta-2,5-diene-4-thione, divinylphosphinic acid, o-ethyl-bis(vinyl)phosphonate, distyrylphosphinic acid, N,N-bis(2-methylprop-1-en-1-yl)aniline, phenyl-(3-phenyl-1-styryl-allyliden)-amine, divinyldimethylsilane and hexa-1,5-diene-3,4-dione.

Other examples of compound of Formula (A) are



.

The step of reacting a compound of Formula (A) with the hypophosphite ester, acid, salt or solvate thereof and the organosilicon compound can result in a first intermediate. It is postulated that the silylphosphorus precursor is added across an alkene such that the hypophosphite is added at geminally di-substituted C of the alkene and is stabilised by the organosilicate moiety. For example, if a phorone is used, the first intermediate can, in general, be represented by Formula (Ai):

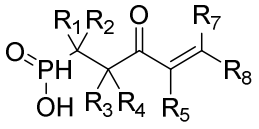


(Ai)

wherein R represents optionally substituted alkyl. When TMSCl or HMDS is used, R is

methyl.

In some embodiments, the first intermediate is treated with an acid to form a second intermediate. For example, following from compound of Formula (Ai), a compound of Formula (Aii) can be obtained:

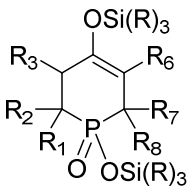


(Aii).

The compound of Formula (Aii) can be isolated after acid work-up. The treatment with acid can be performed at room temperature. For example, the temperature can be of about 15 °C to about 30 °C. The acid can be any organic or inorganic acid. For example HCl can be used. The acid can be selected from HCl (aq), HBr (aq), H_2SO_4, phosphoric acid (H_3PO_4), nitric acid (HNO_3), boric acid (H_3BO_3), methanesulfonic acid, *para*-toluenesulfonic acid, acetic acid, formic acid, citric acid, oxalic acid, tartaric acid, heteropolyacids, or a combination thereof. Excess acid can be used to ensure quantitative hydrolysis of the silyl intermediates as well as neutralisation of any excess base present.

To introduce functionality at R_4 (and subsequently at R_6), the first intermediate (compound of Formula (Ai)) can be reacted with an electrophile. For example, methyl iodide or dimethyl sulphate can be reacted with the first intermediate to introduce a methyl group at R_4 (and subsequently at R_6). Other functionality can be introduced by selection of the electrophile.

In some embodiments, the second intermediate is reacted with an organosilicon compound. The further addition of an organosilicon compound can promote the ring closure reaction. Further advantageously, by splitting up the addition of organosilicon compound into two steps, the synthesis is more controllable in that less by-products is formed. This step can, in general, provide a third intermediate. For example, when phorone is used, the intermediate has a Formula (Aiii):



(Aiii).

In some embodiments, to form a third intermediate (for example as represented by Formula (Aiii)), a molar ratio of the second intermediate to the organosilicon compound is about 1:10, about 1:8, about 1:6, about 1:5, about 1:2, about 1:1.8, about 1:1.7, about 1:1.6, or about 1:1.5, or about 1:1.2, or about 1:1.

Accordingly, if it is desired to form the final product in a single step, the total amount of organosilicon compound required can be added as a single addition. For example, a molar ratio of hypophosphite ester, acid, salt or solvate thereof to the organosilicon compound can be about 1:20 to about 1:2.

In some embodiments, the second intermediate is reacted with the organosilicon compound at a temperature of about 70 °C to about 150 °C. In other embodiments, the temperature is about 80 °C to about 150 °C, about 90 °C to about 150 °C, about 100 °C to about 150 °C, about 110 °C to about 150 °C, or about 120 °C to about 150 °C.

Further advantageously, the higher temperature promotes the ring closure reaction such that a bulky heterocyclyl compound of Formula (I) can be formed.

Accordingly, in some embodiments, if it is desired to form the final product in a single step, the method is firstly performed at room temperature, and subsequently stepping up the temperature to about 70 °C to about 150 °C. In other embodiments, the method is firstly performed at a temperature of about 15 °C to about 30 °C, and subsequently at a temperature of about 70 °C to about 150 °C. The reaction at room temperature can be performed for at least about 1 h to about 24h, or for at least about 1 h to about 48 h. The reaction at the higher temperature can be performed for at least 1 h to about 24 h, or for at least about 1 h to about 48 h.

Similar to the above, the provision of an acid can desilylate the third intermediate.

In some embodiments, the method further comprises a step (b) after step (a) of modifying the compound of formula (I) at the Y moiety. This allows further derivatives to be synthesised and which can be useful in further reactions.

In some embodiments, the method further comprises a step (b) after step (a) of

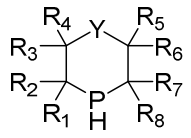
modifying the compound of formula (I) with a protecting group compound. For example, the protecting group compound can be selected from ethylene glycol, methanol, ethanol, propylene glycol, 2,2-dimethyl-1,3-propanediol (neopentylglycol), dimethyl hydrazine, 1,2-ethanedithiol and 1,3-propanedithiol. In some embodiments, a Dean Stark reaction is performed to protect a carbonyl group with an ethylene glycol. A further catalytic amount of an acid can be used. The acid can be selected from HCl (aq), HBr (aq), H_2SO_4, phosphoric acid (H_3PO_4), nitric acid (HNO_3), boric acid (H_3BO_3), methanesulfonic acid, *para*-toluenesulfonic acid, acetic acid, formic acid, citric acid, oxalic acid, tartaric acid, heteropolyacids.

The protection step can be performed at room temperature. For example, the temperature can be of about 15 °C to about 30 °C.

In some embodiments, the method further comprises a step of reducing the compound of formula (I). This reduction step can take place after step (a) or after the modification step (b). The compound of Formula (I) can be at least partially reduced. For example, reductive amination that involves the conversion of a carbonyl group to an amine can be performed. In some embodiments, a Wolff-Kishner reduction of the carbonyl group (ketone) is performed. For example, $NH_2NH_2.H_2O$ in the presence of KOH can be used.

In some embodiments, the method further comprises a step of modifying the compound of Formula (I). For example, the modification can be at the phosphorus atom, in which a phosphaninic acid moiety and/or phosphorinone moiety is modified to its ester, salt or solvate form thereof. For example, compound of Formula (I) can be reacted with oxalyl halide to form phosphaninic halide. Similarly, other moieties such as alkyl, cycloalkyl, aryl, and heteroaryl can be introduced.

In some embodiments, the method further comprises a step (c) after (b) of reducing the phosphorus compound of Formula (I) in order to form a phosphorus compound of Formula (II):

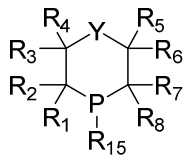


(II)

wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and Y are as disclosed herein.

For example, chlorination using $(COCl)_2$ followed by further reduction ($LiAlH_4$) can give a compound of Formula (II). Further advantageously, this sets up the phosphorus compound to be a readily available synthon equivalent.

In some embodiments, the method further comprises a step of functionalising the compound of Formula (II) in order to form a phosphorus compound of Formula (III):



(III)

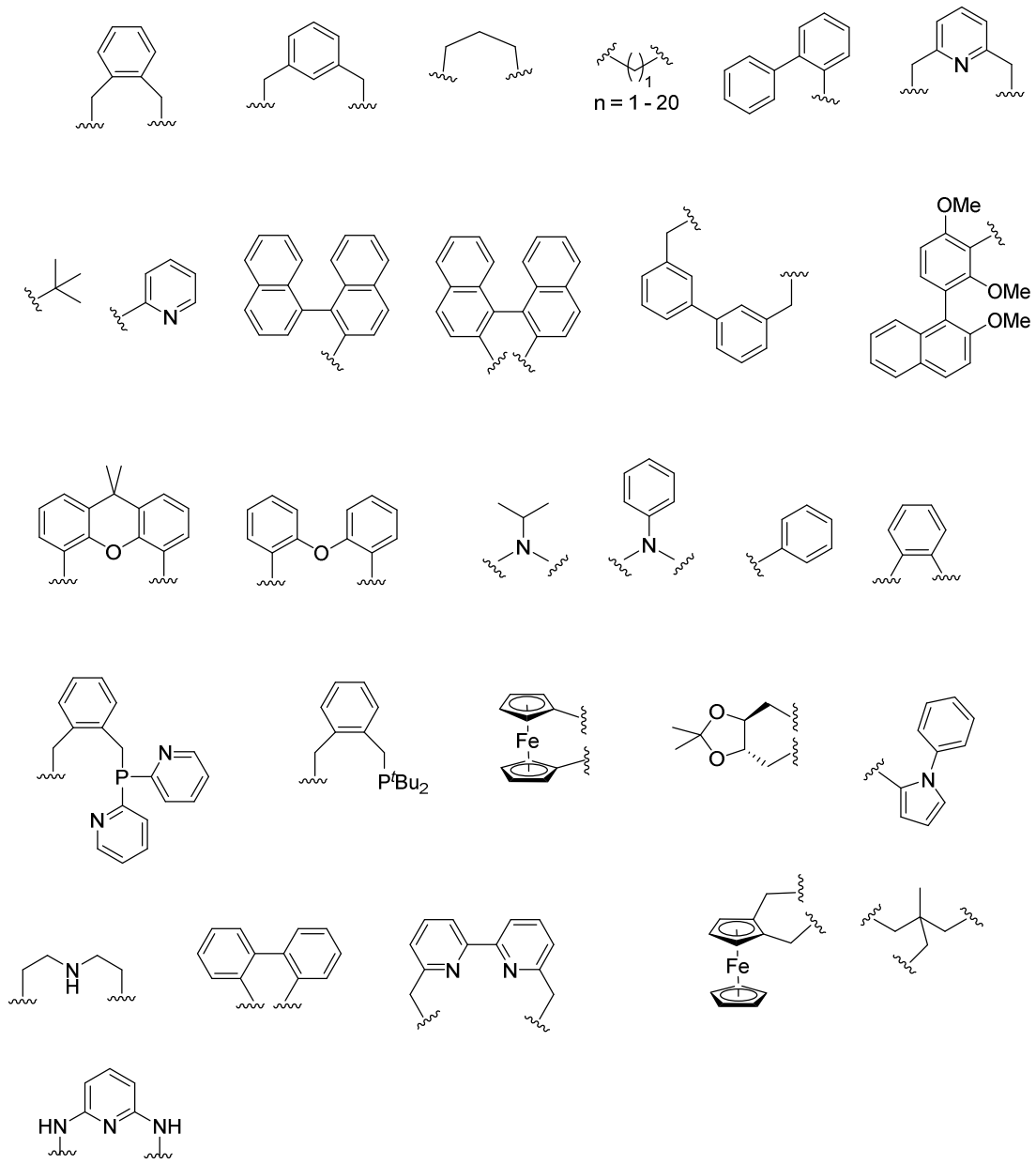
wherein R_1, R_2, R_3, R_4, R_5, R_6 R_7, R_8, R_9, R_{10} and Y are as disclosed herein;

R_{15} is selected from halo, oxo, optionally substituted amino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl.

Compound of Formula (II) can also react with boron compounds to form adducts. An example is shown in Example 8.

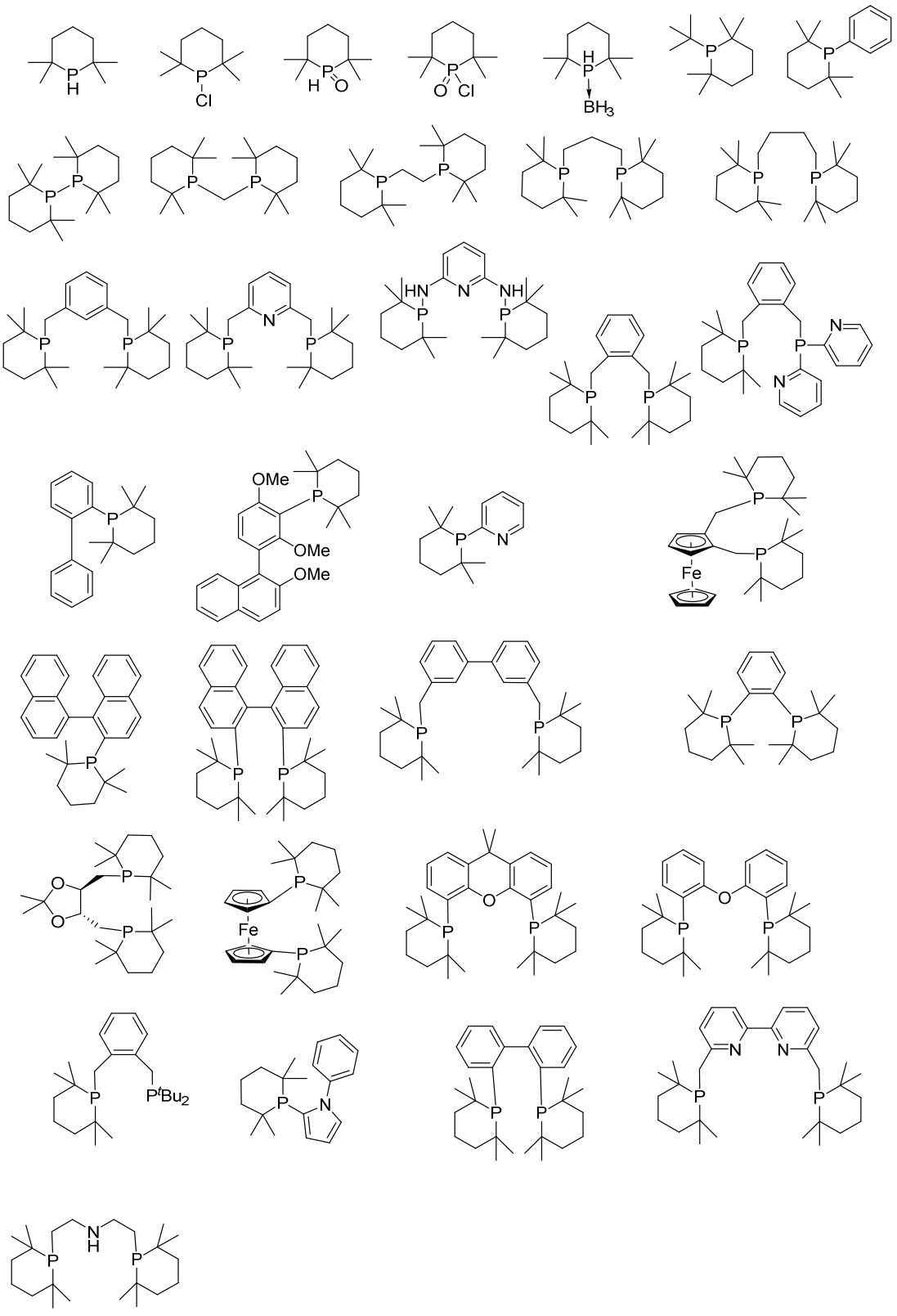
The compound of Formula (III) may be further linked with another compound of Formula (II) to form a dimer. A trimer can also be formed with a third compound of Formula (III). In some embodiments, the optional substituent at R_{15} comprises another compound of Formula (III).

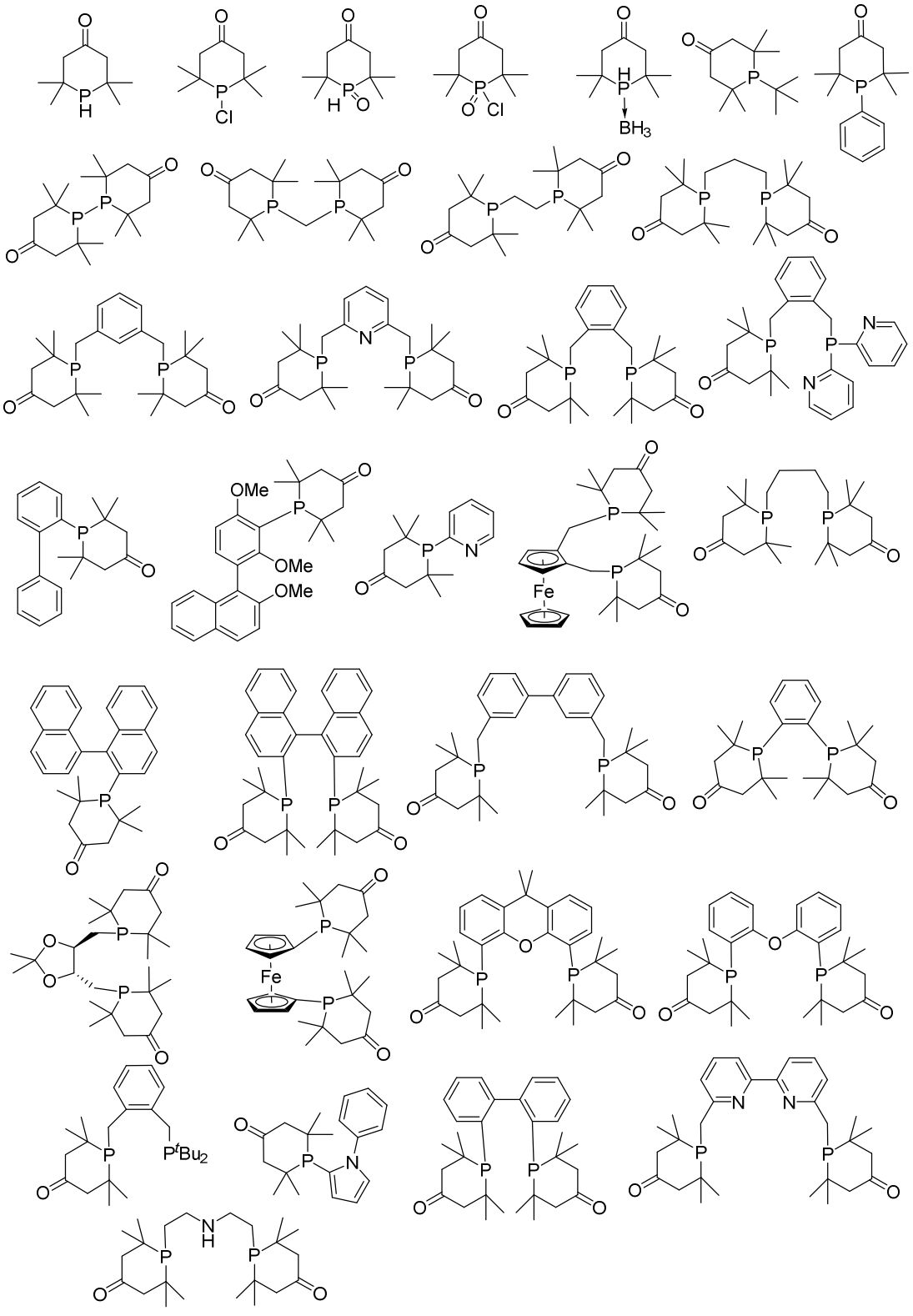
In some embodiments, the optional substituent at R_{15} is selected from:

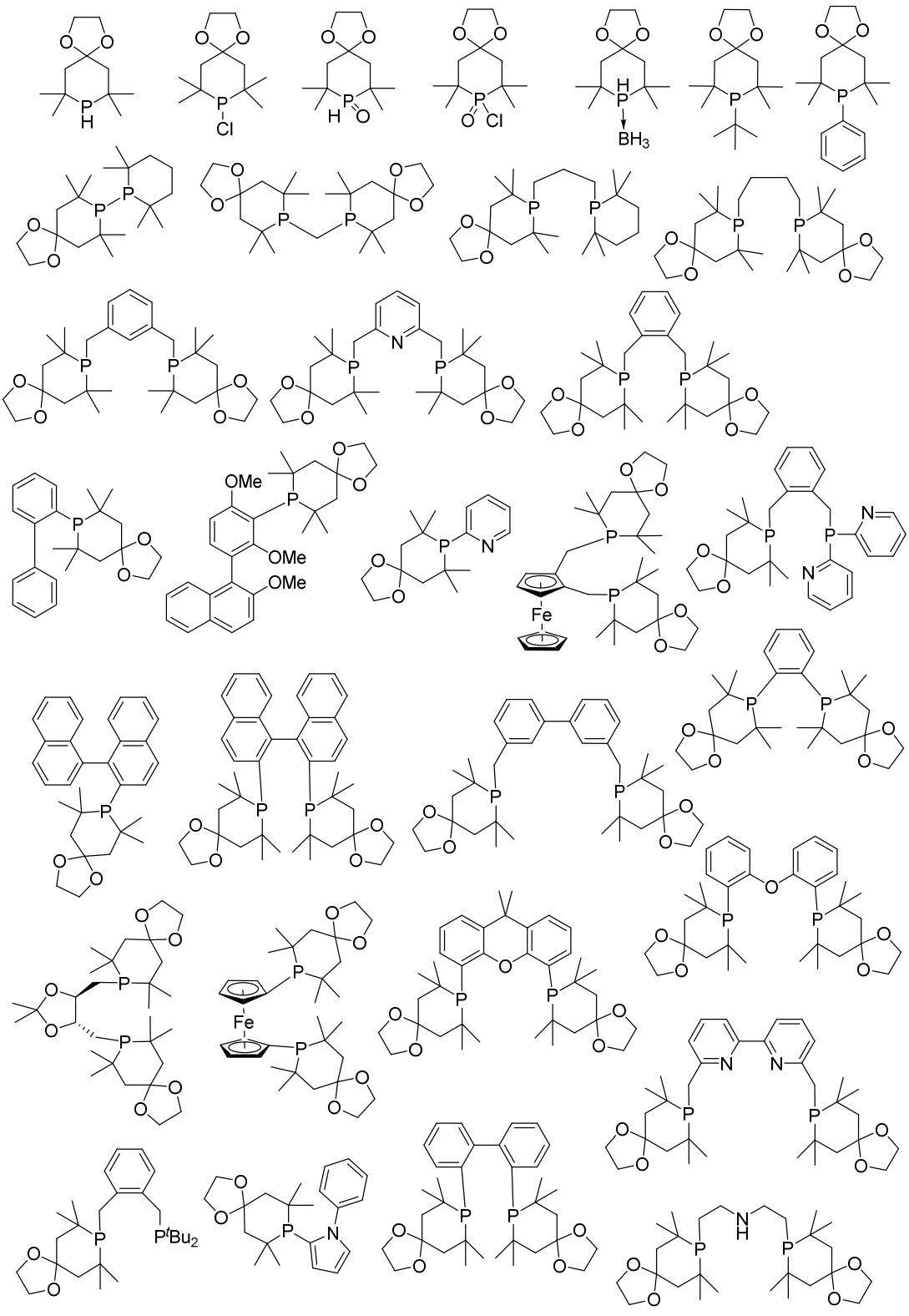


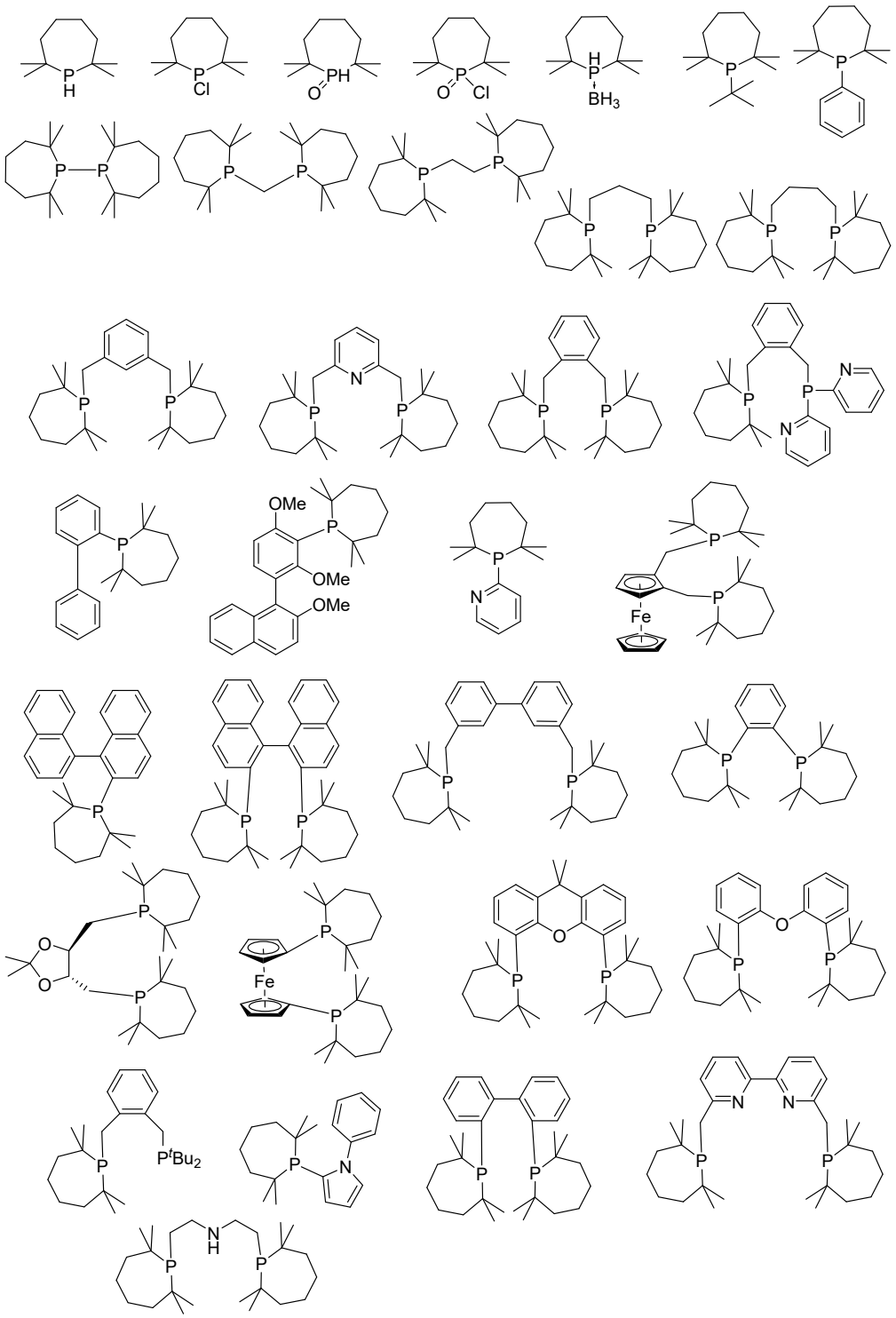
wherein ~~~ represents a bond to R_{15} of compound of Formula (III).

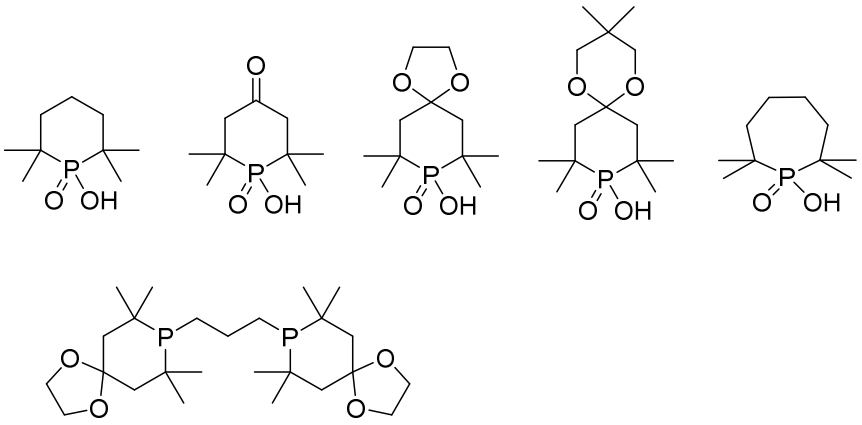
Accordingly, some examples of phosphorus compounds of the present invention include:


P
H
P
Cl
P
H
O
P
O
Cl
H
P
BH3
P
P
P
P
P
P
P
P
P
P
P
P
P
P
HN
N
NH
P
P
P
N
P
P
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P
P
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P
N
P
P
OMe
OMe
OMe
P
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N
P
P
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P
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P
P
P
O
O
P
P
Fe
P
P
O
P
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O
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tBu2
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N
H
P
P



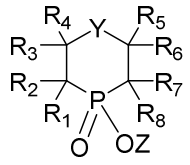



P
H
P
Cl
PH
O
P
O
Cl
H
P
BH3
P
P
P
P
P
P
P
P
P
P
P
P
N
P
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tBu2
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N
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H
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N
P
P



.

The present invention also provides a phosphorus compound of Formula (I), a salt, solvate or isomer thereof:



(I)

wherein Y is selected from an optionally substituted C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene,, optionally substituted silylene, optionally substituted amino, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^{+}(R_9R_{10})-$;

Z is selected from H, optionally substituted alkyl or a metal cation;

R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

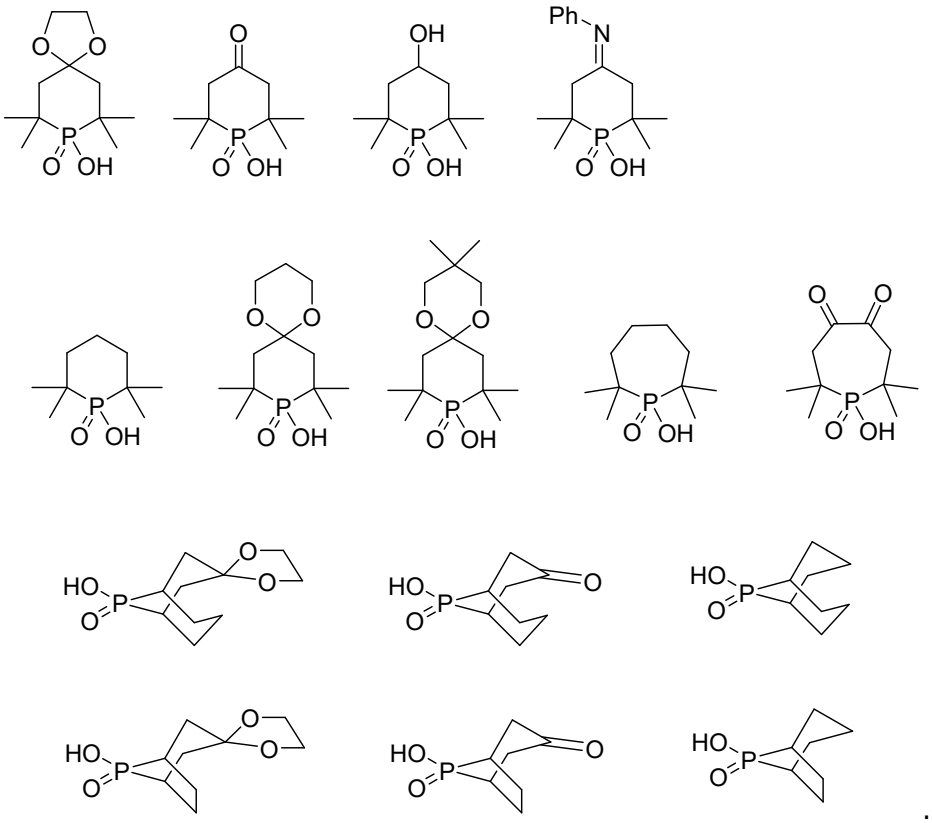
wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;

R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

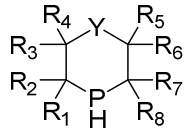
R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl,

optionally substituted heteroaryl.

In some embodiments, the compound of Formula (I) is selected from:



The present invention also provides a phosphorus compound of Formula (II), a salt, solvate or isomer thereof:



(II)

wherein Y is selected from an optionally substituted C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene,, optionally substituted silylene, optionally substituted amino, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^{+}(R_9R_{10})-$;

R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally

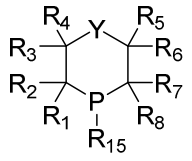
substituted aryl;

wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl.

The compound of Formula (II), a salt, solvate or isomer thereof can be functionalised or dimerised into a compound of Formula (III) a salt, solvate or isomer thereof.

The present invention also provides a phosphorus compound of Formula (III), a salt, solvate or isomer thereof:



(III)

wherein Y is selected from an optionally substituted $C_{1\text{-}10}$ alkylene, optionally substituted $C_{1\text{-}10}$ alkenylene,, optionally substituted silylene, optionally substituted amino, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^+(R_9R_{10})-$;

R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;

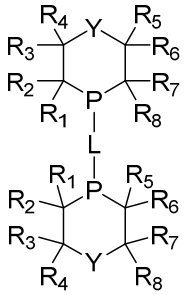
R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted

cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl; and

R_{15} is selected from halo, oxo, optionally substituted amino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl.

The present invention also provides a phosphorus compound of Formula (IIIa), a salt, solvate or isomer thereof:

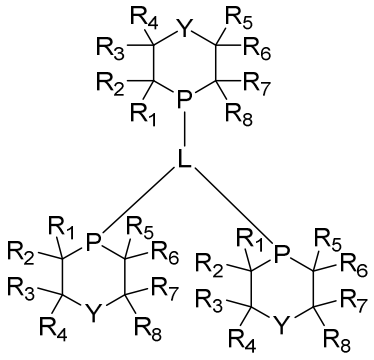


(IIIa)

wherein R_1, R_2, R_3, R_4, R_5, R_6 R_7, R_8, R_9, R_{10} and Y are as disclosed herein;

L is a linker selected from covalent bond, optionally substituted amino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl.

The present invention also provides a phosphorus compound of Formula (IIIb), a salt, solvate or isomer thereof:

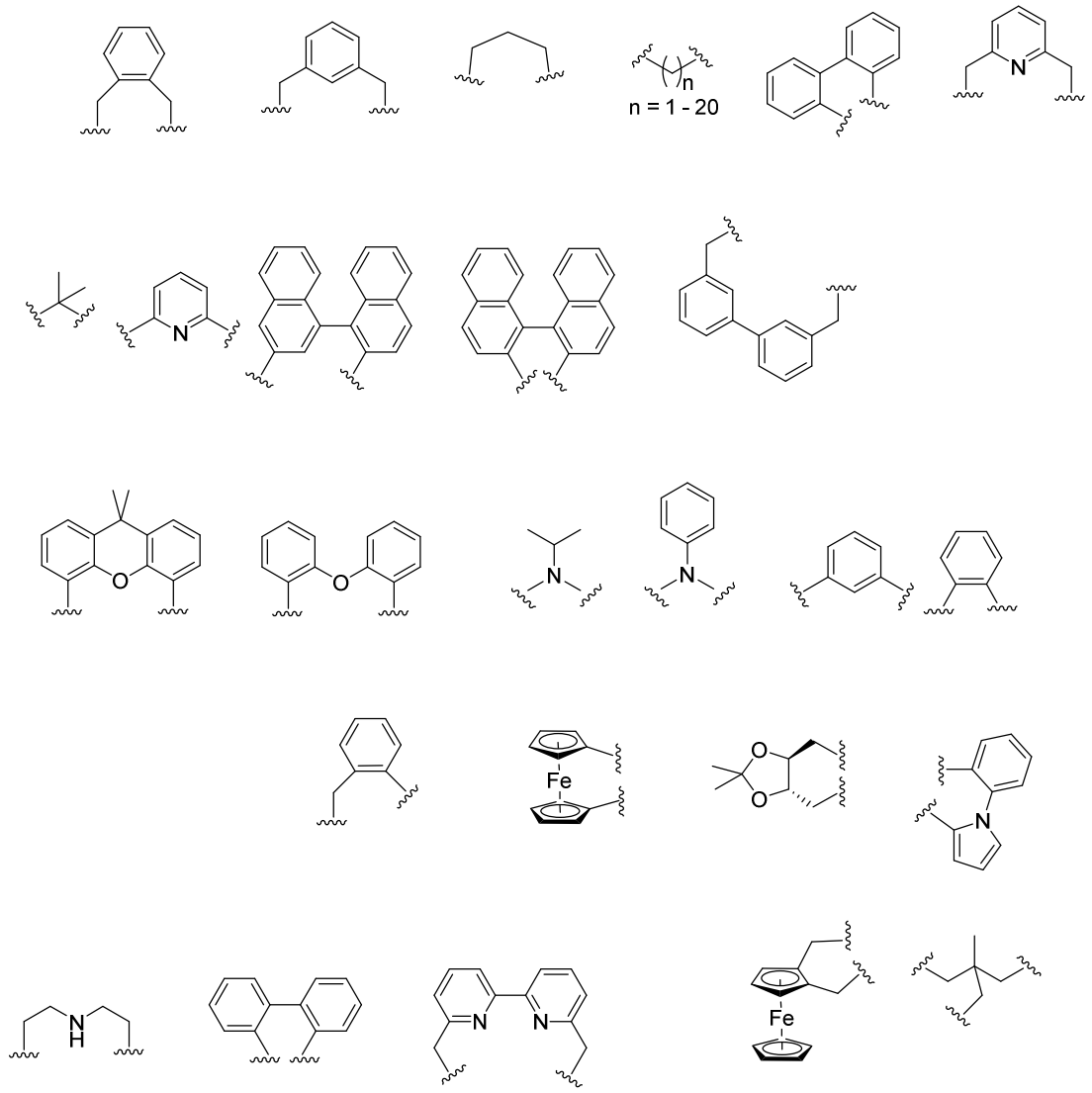


(IIIb)

wherein R_1, R_2, R_3, R_4, R_5, R_6 R_7, R_8, R_9, R_{10} and Y are as disclosed herein;

L is a trivalent linker selected from covalent bond, optionally substituted amino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl.

In some embodiments, L is selected from:



wherein ~~~ represents a bond to L of compound of Formula (IIIa) or (IIIb).

The present invention is industrially applicable in that the production cost of such compounds can be further lowered. For example, the raw materials cost (kg scale) to

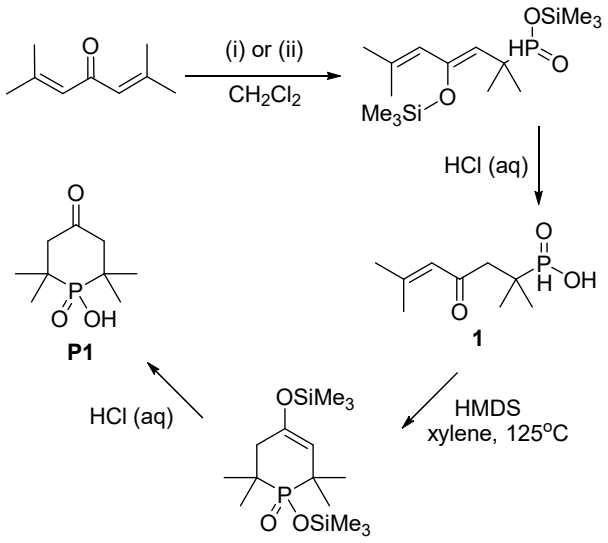
synthesize **TMP** is estimated to be <S$15/g. In comparison, 1 g of the analogous di-*tert*-butyl phosphine from STREM costs S$136. Further, phosphinic acids comprise one of the largest industrial applications and organophosphorus compounds are used in applications such as fire retardants. For example, Clariant's Exolit® OP 1230 is synthesized from diethyl-phosphinic acid.

Examples

2,2,6,6-tetramethylphosphorinic acid (P1)

The synthesis of a secondary cyclic phosphine specialty, 2,2,6,6-tetramethylphosphorinic acid (P1) was achieved according to Scheme 1, starting from an inexpensive, benign phosphorus precursor, ammonium hypophosphite, which was used to generate bis(trimethylsilyl) phosphonite.

Scheme 1. Synthesis of bulky phosphorinic acid P1. (i) Hünigs Base/TMSCl/ $NH_4H_2PO_2$ (ii) HMDS/$NH_4H_2PO_2$.



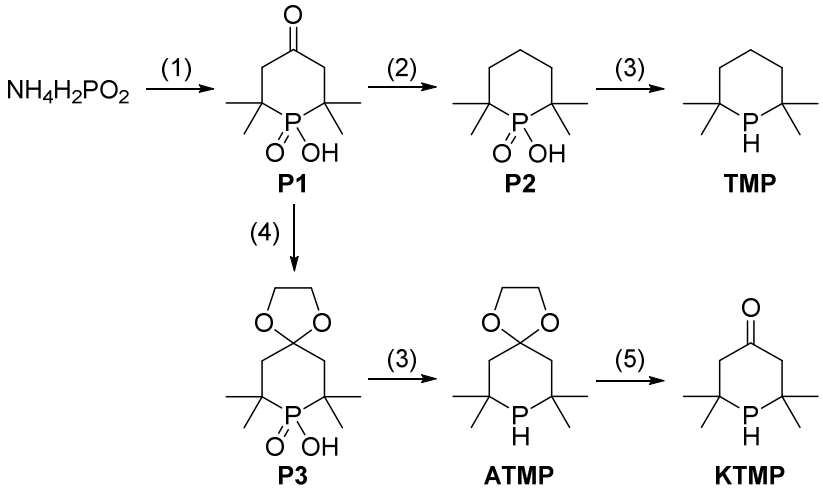
The generated bis(trimethyl)silyl phosphonite was reacted with one equivalent of phorone in a two-step procedure. In the first step the reaction may be conducted at room temperature which after treatment with dilute acid generates the intermediate 1. The second stage ring closing step can be conducted in a solvent with a sufficiently high boiling point such as 1,2-dichloroethane (boiling point = 83.5°C) or more preferably toluene (b.p = 110.6°C) or more preferably xylenes (b.p. ~139°C).

The resulting bulky heterocyclic phosphorinic acid is a useful product in and of itself. Indeed, phosphinic acids themselves are useful chemicals and represent one of the largest application of organophosphorus chemicals (OPCs) in the market (main use: - halogen free flame retardants).

P1 – P3

P1 can be further derivatised through its two functional groups, to generate other products, for example, see Scheme 2.

Scheme 2. Synthesis of phosphorinic acids P1 – P3 and their derivatives.



Conditions:

(1) a. HMDS, b. phorone c. HCl (aq) d. HMDS e. HCl

(2) $NH_2NH_2.H_2O$, KOH, diethylene glycol; 210 °C

(3) a. $(COCl)_2$, cat. DMF b. $LiAlH_4$

(4) ethylene glycol, p-TSA, toluene

(5) HCl, THF

Reduction of the ketone group of P1 generates P2. Further reduction of the phosphinic acid group in P2 generates the secondary phosphine synthon TMP. The ketone group in P1 can also be converted to an acetal group by reaction with ethylene glycol to generate novel P3 which can also be further reduced to generate secondary phosphine ATMP and KTMP. These secondary phosphines can have applications as building blocks for tertiary phosphine ligands by reacting the P-H bond to produce a vast number of derivatives.

Other derivatives of P1 can be envisaged to involve partial reduction of the ketone to an alcohol group, reductive amination of ketone to an amine substituent, use of Michael acceptor analogues of phorone to give different ring substitutions.

Other derivatives

The presently disclosed compounds can also be versatile synthon equivalents used to produce a wide variety of phosphine derivatives (for selected examples see Scheme 1). Phosphine ligands have important application areas in catalysis, such as the Mitsubishi-Lucite process on Jurong Island (Singapore) which employs a bidentate phosphine in the methoxycarbonylation of ethylene. The derivatives tested compare favourably with the commercial ligand on a lab scale (see Table 1).

Scheme 1. Compound derivatives of the present invention

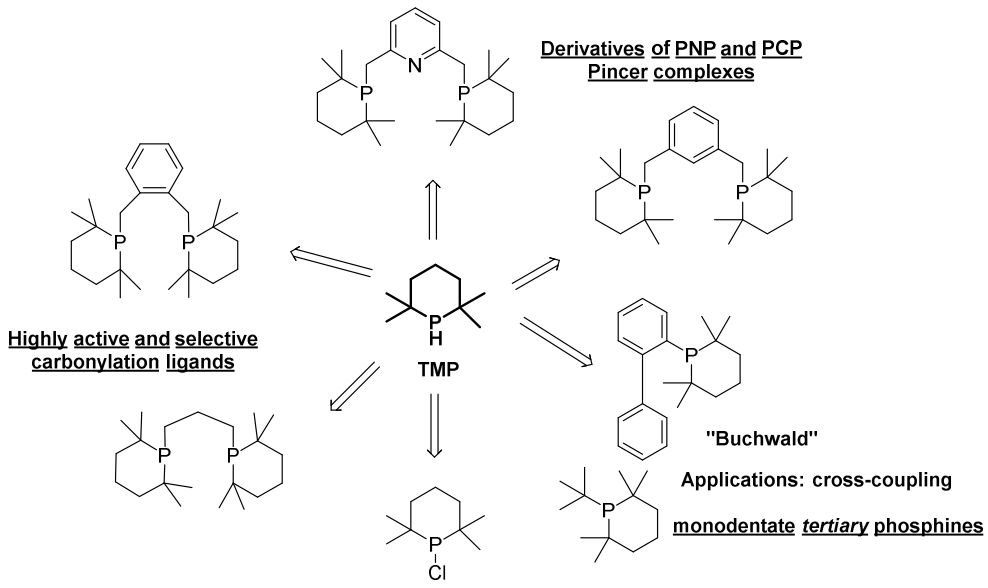
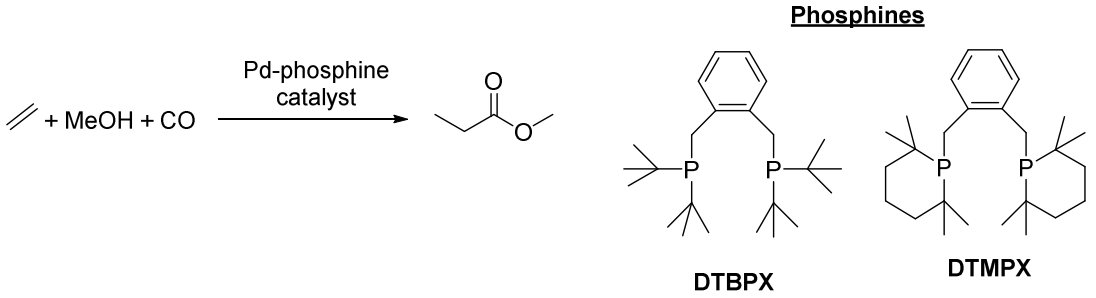
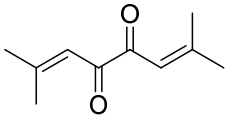


Table 1. Methoxycarbonylation of ethylene (part of Lucite Alpha process).



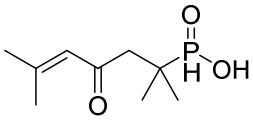
Ligand	Time (mins)	TOF (h^{-1})	Selectivity
DTBPX	10	59,000	>99.0%
DTMPX	10	65,000	>99.0%

Example 1: Synthesis of 2,7-dimethylocta-2,6-diene-4,5-dione.



1,4-Dimethylpiperazine-2,3-dione (3.46 g, 24.3 mmol) was suspended in THF (30 mL) and cooled to 0 °C. 2-Methyl-1-propenylmagnesium bromide (0.68M) (107.4 mL, 73.0 mmol), was added dropwise over 1 hour. After this time the mixture was allowed to warm to room temperature (RT) and stirred for 16 hours. It was then diluted with dilute HCl (aq) (100 mL) and extracted with EtOAc (2 × 100 mL). The combined organic portion was washed with brine (100 mL), dried over $MgSO_4$ and evaporated to give the crude material which was purified by vacuum distillation to give an orange oil. Yield = 2.61 g (65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.81 (2H, br. s, C*H*), 2.24 (6H, s, C*H*$_3$) and 2.00 ppm (6H, s, C*H*$_3$). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 189.6 (s, *C*=O), 162.7 (s, C_q), 117.7 (s, *C*H), 28.6 (s, *C*H$_3$) and 21.5 (s, *C*H$_3$). HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 167.1072; found 167.1065.

Example 2: Synthesis of 2,6-dimethyl-4-oxohept-5-en-2-yl)phosphinic acid.

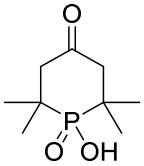


Method A: Hexamethyldisilazane (47.2 g, 292.5 mmol) and ammonium hypophosphite (23.4 g, 281.3 mmol) were stirred for 3 hours at 110 °C until evolution of ammonia had finished. This resulted in a clear solution with traces of white solid that had sublimed on

the top half of the flask. The mixture was cooled to RT and phorone (31.1 g, 225.0 mmol) dissolved in CH_2Cl_2 (120 mL) was added and the mixture stirred at RT for 24 hours. After this time HCl (aq) (2.0M, 100 mL) was added and the mixture stirred vigorously, which dissolved the white insoluble salts that had precipitated. The organic layer was then separated and dried ($MgSO_4$) to give a yellow oil. Yield = 42.7 g (93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.05 (1H, s, OH), 7.07 (1H, d, $^1J_{HP}$ = 565.0 Hz, P*H*), 6.01 (1H, s, C*H*), 2.62 (2H, d, $^2J_{HP}$ = 14.1 Hz, CH_2), 2.09 (3H, s, =CCH_3), 1.84 (3H, s, =CCH_3) and 1.17 ppm (6H, d, $^2J_{HP}$ = 17.8 Hz, PC(CH_3)$_2$. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 198.7 (s, *C*=O), 156.6 (s, $(CH_3)_2C$=CH-), 124.1 (s, $(CH_3)_2$C=*C*H-), 50.0 (s, CH_2), 33.7 (d, $^1J_{CP}$ = 95.6 Hz, -P*C*$(CH_3)_2$), 27.8 (s, ($CH_3)_2$C=CH-), 20.6 (d, $^2J_{CP}$ = 56.6 Hz, PC($CH_3)_2$) and 20.3 ppm (s, ($CH_3)_2$C=CH-). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 46.8 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 205.0994; found 205.0984. Elem. Anal. Calcd for $C_9H_{17}O_3P$: C, 52.94; H, 8.39. Found: C, 52.37; H, 8.47.

Method B: Ammonium hypophosphite (0.5 g, 6.0 mmol) in CH_2Cl_2 (20 mL) was cooled to 0 °C. *N,N*-Diisopropylethylamine (Hünigs base) (2.7 g, 3.5 mL, 21.1 mmol) was added and the mixture stirred at 0 °C for 1 hour. After this time trimethylsilyl chloride (2.3 g, 2.7 mL, 21.1 mmol) was added, HCl fumes were observed and the solution became colorless. After stirring for 4 hours, phorone (0.83 g, 0.92 mL, 6.0 mmol) in CH_2Cl_2 (1.0 mL) was added and stirred at 0 °C for 2 hours before being allowed to warm to RT. After 48 hours the mixture was passed through celite and washed with HCl (10%, aq) (20 mL × 2) followed by deionized (DI) H_2O (20 mL). The organic fraction was separated and dried ($MgSO_4$), then the volatiles were removed *in vacuo* to give a yellow oil. Yield = 0.44 g (36%). The compound characterization was consistent with that obtained using method A.

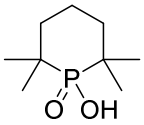
Example 3: Synthesis of 2,2,6,6-tetramethylphosphorinic acid.



(2,6-Dimethyl-4-oxohept-5-en-2-yl)phosphinic acid (22.1 g, 108.0 mmol) and hexamethyldisilazane (20.9 g, 130.0 mmol) was stirred in degassed xylenes (500 mL) for 72 hours at 125 °C, giving a clear pale yellow solution. To the reaction mixture, 0.4 equivalents of hexamethyldisilazane (7.0 g, 43.2 mmol) was added and the mixture stirred for 24 hours. The reaction mixture was cooled to RT. Subsequently HCl (aq, 2.0M)

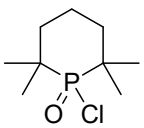
(200 mL) was added and the mixture stirred vigorously. The aqueous layer was then separated and the organic layer was extracted a second time with HCl (aq) (2.0M, 50 mL). The combined aqueous layer was backwashed with CH_2Cl_2 (5 × 50 mL). The combined CH_2Cl_2 extracts were dried over $MgSO_4$ to give an off-white solid. The xylene phase was evaporated via rotary evaporator to give an off-white solid. Total combined yield from both organic phases = 12.9 g (58%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.6 (1H, s, O*H*), 2.57 (4H, d, $^3J_{HP}$ = 15.7 Hz, C*H*$_2$) and 1.28 ppm (12H, d, $^3J_{HP}$ = 13.7 Hz, C*H*$_3$). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 206.8 (d, $^3J_{CP}$ = 9.9 Hz, *C*=O), 53.7 (s, *C*H_2), 36.5 (d, $^1J_{CP}$ = 86.0 Hz, *C*$(CH_3)_2$ and 24.1 ppm (d, $^2J_{CP}$ = 1.8 Hz, *C*H_3). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 58.1 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 205.0994; found 205.0985. Elem. Anal. Calcd for $C_9H_{17}O_3P$: C, 52.94; H, 8.39. Found: C, 52.40; H, 8.33.

Example 4: Synthesis of 2,2,6,6-tetramethylphosphaninic acid.



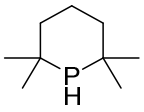
2,2,6,6-Tetramethylphosphorinic acid (8.5 g, 41.8 mmol) was suspended in diethylene glycol (120 mL). KOH (11.7 g, 209.1 mmol) and hydrazine monohydrate (65 wt%, aq) (16.1 g, 15.6 mL) were added and the mixture heated to 150 °C using a dean & stark trap to remove H_2O. The temperature was gradually increased to 210 °C and maintained for 16 hours. Upon cooling the mixture was diluted with DI H_2O (100 mL), acidified with HCl (aq, 2.0M) to pH 1 and then extracted with CH_2Cl_2 (3 × 80 mL). The combined organic extracts were then washed with brine, dried and evaporated to give a white solid. Yield = 6.1 g (77 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.38 (1H, br. s, O*H*), 1.67 – 1.51 (6H, m, C*H*$_2$) and 1.20 ppm (12H, d, $^3J_{HP}$ = 13.8 Hz, C*H*$_3$). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 39.5 (s, C_q*C*H_2), 34.1 (d, $^1J_{CP}$ = 82.7 Hz, *C*$(CH_3)_2$), 23.7 (s, *C*H_3) and 19.2 ppm (d, $^3J_{CP}$ = 9.0 Hz, -*C*H_2-). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 62.4 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 191.1201; found 191.1197. Elem. Anal. Calcd for $C_9H_{19}O_2P$: C, 56.83; H, 10.07. Found: C, 56.43; H, 9.87.

Example 5: Synthesis of 2,2,6,6-tetramethylphosphaninic chloride.



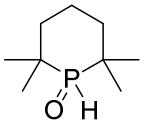
2,2,6,6-Tetramethylphosphaninic acid (1.25 g, 6.6 mmol) was dissolved in degassed CH_2Cl_2 (15 mL). Dimethylformamide (DMF) (5 drops) was added and oxalyl chloride (4.2 g, 32.8 mmol) was added dropwise into the reaction flask. Effervescence was observed. The reaction mixture was then stirred for 48 hours to give a clear yellow solution. The reaction mixture was dried *in vacuo* to obtain a brown oil. The product was extracted with pentane to give a brown oil. Yield = 1.1g (81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.81 – 1.51 (6H, m, C*H*$_2$), 1.36 (6H, d, $^3J_{HP}$ = 15.8 Hz, C*H*$_3$) and 2.60 ppm (6H, d, $^3J_{HP}$ = 16.7 Hz, C*H*$_3$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 40.2 (d, $^1J_{CP}$ = 59.7 Hz, *C*(*C*H$_3$)$_2$), 39.3 (s, C$_q$*C*H$_2$), 25.8 (d, $^2J_{CP}$ = 1.9 Hz, *C*H$_3$), 23.5 (s, *C*H$_3$) and 18.8 ppm (d, $^3J_{CP}$ = 8.9 Hz, -*C*H$_2$-). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 87.8 ppm. HR-MS (+ve ESI): m/z (calc.) [M+H]$^+$ 209.0862; found 209.0854. Elem. Anal. Calcd for $C_9H_{18}ClOP$: C, 51.80; H, 8.70. Found: C, 48.41; H, 8.52.

Example 6: Synthesis of 2,2,6,6-tetramethylphosphinane, TMP.



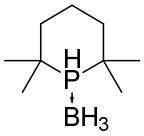
$LiAlH_4$ (3.5 g, 92.0 mmol) was suspended in diethyl ether (Et_2O) (120 mL) and cooled to 0 °C. 2,2,6,6-Tetramethylphosphaninic chloride (8.0 g, 38.3 mmol) in Et_2O (20 mL) was added dropwise over 15 minutes. After the addition the mixture was allowed to warm to RT and stirred for 16 hours. It was quenched by addition of NaOH (aq. 20%), (7 mL) at 0 °C, followed by addition of DI H_2O (5 mL). Drying agent ($MgSO_4$) was added and the mixture was filtered. The Et_2O was removed by distillation under argon. Finally, the phosphine was purified *via* vacuum transfer giving a colourless liquid. Yield = 2.8 g (46%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.60 (1H, d of sept. $^1J_{PH}$ = 200.1 Hz, and $^3J_{HP}$ = 1.5 Hz, P*H*), 1.64 – 1.50 (4H, m, C*H*$_2$), 1.23 – 1.13 (2H, m, C*H*$_2$), 1.03 (6H, dd, $^3J_{PH}$ = 15.3 Hz and $^4J_{HH}$ = 1.2 Hz, C*H*$_3$) and 0.94 ppm (6H, d, $^3J_{PH}$ = 14.1 Hz, C*H*$_3$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 43.4 (d, $^2J_{CP}$ = 6.4 Hz, C$_q$*C*H$_2$), 32.6 (d, $^2J_{CP}$ = 13.7 Hz, *C*H$_3$). 27.7 (d, $^1J_{CP}$ = 8.9 Hz, *C*(CH$_3$)$_2$), 26.4 (d, $^2J_{CP}$ = 25.1 Hz, *C*H$_3$) and 20.9 ppm (s, -*C*H$_2$-). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ −9.1 ppm. HR-MS (+ve ESI): m/z (calc.) [M+H]$^+$ 159.1303; found 159.1297.

Example 7: Synthesis of 2,2,6,6-tetramethylphosphinane 1-oxide, TMP=O.



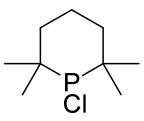
TMP (0.20 g, 1.26 mmol) was dissolved in CH_2Cl_2 (3 mL) and cooled to 0 °C. *m*-CPBA (70%, aq) (0.22 g, 1.26 mmol) in CH_2Cl_2 (5 mL) was added slowly. After 1 hour the mixture was allowed to warm to RT and stirred for an additional hour. After this time an aliquot of CH_2Cl_2 (10 mL) was added and the mixture washed with saturated $NaHCO_3$ (aq) (2 × 10 mL). The combined aqueous portion was then backwashed with CH_2Cl_2 (15 mL). The combined organic phases were dried over $MgSO_4$, filtered and evaporated to yield hydroscopic colourless platelets. Yield = 0.15 g (68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.18 (1H, d, $^1J_{HP}$ = 429.8 Hz, P*H*), 1.71 – 1.36 (6H, m, C*H*$_2$), 1.24 (6H, s, $^3J_{HP}$ = 15.3 Hz, C*H*$_3$) and 1.24 ppm (6h, d, $^3J_{HP}$ = 12.3 Hz, C*H*$_3$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 39.3 (d, $^2J_{CP}$ = 2.1 Hz, C_q*C*H$_2$), 33.7 (d, $^1J_{CP}$ = 58.0 Hz, *C*(CH$_3$)$_2$), 27.7 (d, $^2J_{CP}$ = 1.2 Hz, *C*H$_3$), 20.0 (s, *C*H$_3$) and 18.9 ppm (d, $^3J_{CP}$ = 7.6 Hz, -*C*H$_2$-). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 59.2 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 175.1252; found 175.1242. Elem. Anal. Calcd for $C_9H_{19}OP$: C, 62.05; H, 10.99. Found: C, 62.58; H, 10.77.

Example 8: Synthesis of 2,2,6,6-tetramethylphosphinane borane complex.



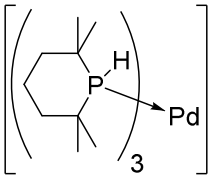
Borane dimethyl sulfide complex (2.0M in THF, 2.0 mL, 4.0 mmol) was added to TMP (0.6 g, 3.8 mmol) in THF (10 mL). After stirring for 2 hours the volatiles were removed *in vacuo* to yield a white solid. Yield = 0.6 g (92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.98 (1H, d of m, $^1J_{HP}$ = 318.1 Hz, P*H*), 1.83 – 1.55 (4H, m, C*H*$_2$), 1.50 – 1.40 (2H, m, C*H*$_2$), 1.20 (6H, d, $^3J_{HP}$ = 14.2 Hz, C*H*$_3$), 1.19 (6H, d, $^3J_{HP}$ = 15.5 Hz, C*H*$_3$) and 0.43 ppm (3H, br. q, $^1J_{HB}$ = 99.2 Hz, B*H*$_3$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 41.8 (d, $^2J_{CP}$ = 5.2 Hz, C_q*C*H$_2$), 30.2 (d, $^2J_{CP}$ = 1.7 Hz, *C*H$_3$), 28.0 (d, $^1J_{CP}$ = 29.4 Hz, *C*(CH$_3$)$_2$), 22.0 (d, $^2J_{CP}$ = 7.4 Hz, *C*H$_3$) and 19.4 ppm (d, $^3J_{CP}$ = 4.8 Hz, -*C*H$_2$-). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 34.3 ppm (q, $^1J_{HB}$ = 46.1 Hz). HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 173.1630; found 173.1644. Elem. Anal. Calcd for $C_9H_{22}BP$: C, 62.83; H, 12.89. Found: C, 61.50; H, 12.60.

Example 9: Synthesis of 1-chloro-2,2,6,6-tetramethylphosphinane



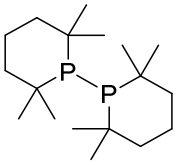
TMP (1.70 g, 10.7 mmol) was dissolved in THF (5.0 mL) and methyl trichloroacetate (1.91 g, 10.7 mmol) was added. The mixture was stirred for 16 hours whereupon the by-product methyl 2,2-dichloroacetate was removed *in vacuo* to give a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.79 – 1.65 (2H, m, C*H*$_2$), 1.64 – 1.47 (2H, m, C*H*$_2$), 1.39 – 1.29 (2H, m, C*H*$_2$), 1.18 (6H, d, $^{3}J_{HP}$ = 18.1 Hz, C*H*$_3$) and 1.15 ppm (6H, d, $^{3}J_{HP}$ = 11.5 Hz, C*H*$_3$). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 34.2 (br. s, C_qCH_2), 33.3 (d, $^{1}J_{CP}$ = 32.7 Hz, *C*$(CH_3)_2$), 30.1 (d, $^{2}J_{CP}$ = 8.4 Hz, *C*H_3), 25.5 (d, $^{2}J_{CP}$ = 33.6 Hz, *C*H_3) and 19.8 ppm (s, -$CH_2CH_2CH_2$-). $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 130.5 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 193.0913; found 193.0903. Elem. Anal. Calcd for $C_9H_{18}ClP$: C, 56.11; H, 9.42. Found: C, 54.53; H, 9.11.

Example 10: Synthesis of $[(TMP)_3Pd^{(0)}]$.



TMP in acetone (1 mL) was cooled to 0 °C. A deep red solution of allyl(cyclopentadienyl)palladium(II) in acetone (1 mL) was added dropwise with a colour change to yellow. After the addition the mixture was stirred for 30 mins. The yellow solid that had formed was filtered and dried *in vacuo*. Yield = 90 mg (67%). ^{1}H NMR (400 MHz, C_6D_6): δ 4.15 (3H, d, $^{1}J_{PH}$ = 255.7 Hz, P*H*), 1.84 – 1.63 (9H, m, C*H*$_2$), 1.56 – 1.46 (3H, m, C*H*$_2$), 1.44 – 1.33 (6H, m, C*H*$_2$) and 1.35 – 1.18 ppm (36H, m, C*H*$_3$). $^{13}C\{^{1}H\}$ NMR (101 MHz, C_6D_6): δ 43.8 (s, C_qCH_2), 33.6 (s, *C*H_3), 32.1 (s, *C*H_3), 26.0 (d, $^{1}J_{CP}$ = 9.9 Hz, *C*$(CH_3)_2$) and 21.1 (s, $CH_2CH_2CH_2$). ^{31}P NMR (162 MHz, C_6D_6): δ 42.1 ($^{1}J_{PH}$ = 256 Hz) ppm. Elem. Anal. Calcd for $C_{27}H_{57}P_3Pd$: C, 55.81; H, 9.89. Found: C, 55.54; H, 9.49.

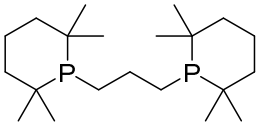
Example 11: Synthesis of 2,2,2',2',6,6,6',6'-octamethyl-1,1'-biphosphinane



n-BuLi (2.0M in cyclohexane) (0.70 mL, 1.39 mmol) was added dropwise to a solution of TMP (0.20 g, 1.26 mmol) in THF (2 mL) at −78°C. The mixture was allowed to warm to RT and stirred for one hour. The mixture was cooled to −78°C and dibromoethane

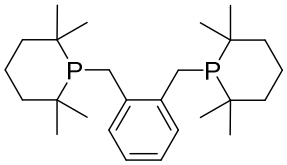
(0.11 g, 0.57 mmol) in THF (2 mL) was added dropwise. The mixture was then allowed to warm to RT and stirred for 16 hours. After this time the volatiles were removed *in vacuo* and the crude solid was extracted with pentane (2 × 10 mL). The pentane was evaporated to yield a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.92 – 1.29 (12H, m, C*H*$_2$), 1.48 (12H, br. s, C*H*$_3$) and 1.19 ppm (12H, t, $^{3}J_{CP}$ = 9.0 Hz, C*H*$_3$). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 45.3 (t, $|^{2}J_{CP} + {}^{3}J_{CP}|$ = 6.8 Hz, C_qCH_2), 33.4 (t, $|^{1}J_{CP} + {}^{2}J_{CP}|$ = 15.0 Hz,), 33.3 (t, $|^{2}J_{CP} + {}^{3}J_{CP}|$ = 9.0 Hz, *C*H$_3$), 28.2 (s, *C*H$_3$) and 20.3 ppm (s, -*C*H$_2$-). $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 19.1 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 315.2371; found 315.2466.

Example 12: Synthesis of 1,3-bis(2,2,6,6-tetramethylphosphinan-1-yl)propane, BTMPPr



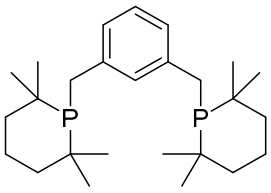
TMP (1.0 g, 6.32 mmol) was dissolved in THF (15 mL). ^{n}BuLi (2.0M in cyclohexane, 3.5 mL, 6.95 mmol) was added dropwise at −78 °C and allowed to warm to RT. 1,3-Dibromopropane (0.57 g, 2.84 mmol) was dissolved in THF and added dropwise at −78 °C and allowed to warm to RT and stirred for 16 hours. After this time the volatiles were removed *in vacuo* to give a dark olive green oil. The crude product was extracted with pentane (2 × 20 mL), passed through a glass filter and the volatiles removed *in vacuo* to give an off-white waxy solid. The product was then dissolved in CH_2Cl_2 (10 mL) and filtered through a plug of silica. The volatiles were removed *in vacuo* to yield a translucent oil. Yield = 0.96 g (95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.08 – 1.33 (18H, m, *CH*$_2$), 1.10 (12H, d, $^{3}J_{HP}$ = 17.0 Hz, C*H*$_3$) and 1.04 ppm (12H, d, $^{3}J_{HP}$ = 6.7 Hz, C*H*$_3$). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 40.2 (br s, C_qCH_2), 31.5 (d, $^{2}J_{CP}$ = 26.4 Hz, *C*H$_3$), 29.1 (d, $^{2}J_{CP}$ = 14.7 Hz, *C*(CH$_3$)$_2$), 28.8 (t, $^{2}J_{CP}$ = 22.8 Hz, -*C*H$_2$CH$_2$P), 26.2 (br s, *C*H$_3$), 22.7 (dd, $^{1}J_{CP}$ = 22.4 Hz, $^{3}J_{CP}$ = 12.6 Hz, *C*H$_2$P) and 20.4 ppm (s, $C_qCH_2CH_2CH_2$). $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 8.04 ppm. Elem. Anal. Calcd for $C_{21}H_{42}P_2$: C, 70.75; H, 11.87. Found: C, 70.56; H, 11.84.

Example 13: Synthesis of 1,2-bis((2,2,6,6-tetramethylphosphinan-1-yl)methyl)benzene, BTMPX



^{n}BuLi (2.0M in cyclohexane, 1.9 mL, 3.84 mmol) was slowly added to 2,2,6,6-tetramethylphosphinane borane complex (0.6 g, 3.49 mmol) at −78 °C and allowed to warm to RT. After stirring for 1 hour, 1,5-dihydrobenzo[e][1,3,2]dioxathiepine 3,3-dioxide was dissolved in THF (2.5 mL) and added dropwise into the reaction mixture at −78 °C , the reaction mixture was allowed to warm to RT and stirred for 16 hours. The resulting yellow solution was dried *in vacuo* to give a yellow-white solid. The crude product was washed with methanol and dried *in vacuo.* It was then taken up in CH_2Cl_2 (50 mL) and washed with H_2O (2 × 50 mL). Pyrrolidine (5 mL) was added and then the mixture was heated to 55 °C for 16 hours. The volatiles were removed *in vacuo* to give a white solid. The product was then recrystallized from MeOH to yield white crystals. Yield = 0.49 g (75 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.37 (2H, m, ArH), 7.09 – 7.01 (2H, m, ArH), 3.09 (4H, s, C*H*$_2$), 1.62 – 1.40 (12H, m, CH_2), 1.18 (12H, d, $^{3}J_{HP}$ = 4.88 Hz, C*H*$_3$) and 0.92 ppm (12H, d, $^{3}J_{HP}$ = 17.5 Hz, C*H*$_3$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 138.1 (dd, $^{2}J_{CP}$ = 7.5 Hz, $^{3}J_{CP}$ = 2.9 Hz, Ar*C*$_q$), 131.2 (d, $^{3}J_{CP}$ = 40.4 Hz, Ar*C*), 125.6 (d, $^{4}J_{CP}$ = 1.7 Hz, Ar*C*), 41.8 (br. s., *C*H_2CH_2CH_2), 32.0 (d, $^{2}J_{CP}$ = 25.8 Hz, *C*H_3), 30.1 (d, $^{1}J_{CP}$ = 17.8 Hz, *C*$(CH_3)_2$), 26.1 (dd, $^{1}J_{CP}$ = 26.8 Hz, $^{4}J_{CP}$ = 7.4 Hz, *C*H_2P), 24.9 (br. s., *C*H_3) and 20.4 ppm (d, $^{3}J_{CP}$ = 1.8 Hz, CH_2*C*H_2CH_2). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 10.2 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 419.2997; found 419.2993. Elem. Anal. Calcd for $C_{26}H_{44}P_2$: C, 74.61; H, 10.60. Found: C, 74.03; H, 10.42.

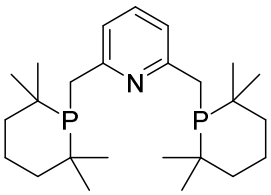
Example 14: Synthesis of 1,3-bis((2,2,6,6-tetramethylphosphinan-1-yl)methyl)benzene, ^{TMP}(PCP)



TMP (0.30 g, 1.89 mmol) and α,α'-dibromo-*m*-xylene (0.23 g, 0.85 mmol) were mixed together in MeOH (8 mL). After stirring for 16 hours, triethylamine (NEt_3) (0.20 g, 0.26 mL, 1.89 mmol) was added giving a white precipitate which was filtered and dried. A second crop was obtained by placing the filtrate in the freezer at −20 °C. ^{1}H NMR (400 MHz, $CDCl_3$): 7.30 (1H, br s, Ar*H*), 7.14 (3H, br s, Ar*H*), 2.80 (4H, d, $^{2}J_{HP}$ = 1.9 Hz,

C*H*$_2$), 1.66 – 1.34 (12H, m, C*H*$_2$), 1.13 (12H, d, $^3J_{HP}$ = 5.3 Hz, C*H*$_3$), 0.93 (12H, d, $^3J_{HP}$ = 17.4 Hz, C*H*$_3$). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): 140.5 (d, $^3J_{CP}$ = 9.8 Hz, Ar*C*), 130.7 (t, $^4J_{CP}$ = 7.2 Hz, Ar*C*), 128.3 (s, Ar*C*), 126.9 (dd, $^2J_{CP}$ = 8.1 Hz, $^4J_{CP}$ = 2.1 Hz, ArC_q), 41.1 (br s, *C*H$_2$), 31.6 (d, $^1J_{CP}$ = 25.8 Hz, *C*(CH$_3$)$_2$), 29.8 (d, $^2J_{CP}$ = 16.9 Hz, *C*H$_3$), 27.7 (d, $^1J_{CP}$ = 25.2 Hz, *C*H$_2$P), 25.4 (br s, *C*H$_3$) and 20.4 ppm (d, $^3J_{CP}$ = 1.6 Hz, CH$_2$*C*H$_2$CH$_2$). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): 16.7 δ ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 419.2297; found 419.2290. Elem. Anal. Calcd for $C_{26}H_{44}P_2$: C, 74.61; H, 10.60. Found: C, 73.81; H, 10.43.

Example 15: Synthesis of 2,6-Bis((2,2,6,6-tetramethylphosphinan-1-yl)methyl)pyridine, ^{TMP}(PNP)



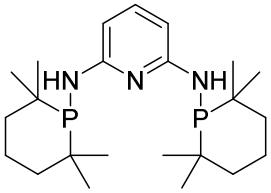
Method A: 2,6-Lutidine (0.13 g, 0.14 mL, 1.2 mmol) was dissolved in Et$_2$O (2 mL) and the mixture cooled to 0 °C. ^{n}BuLi (2.0 M in hexanes, 1.4 mL, 2.8 mmol) was added dropwise. The orange mixture was heated at 40 °C for 20 hours. After this time it was cooled to −78 °C and 1-chloro-2,2,6,6-tetramethylphosphinane (0.50 g, 2.6 mmol) in Et$_2$O (1 mL) was added dropwise. The dark brown mixture was allowed to warm to RT. MeOH (6 mL) was added then the volatiles were removed *in vacuo*. Et$_2$O was added (4 mL) and the mixture was then passed through a glass filter, then evaporated to yield a crude orange solid. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 17.4 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 420.2949; found 420.2941.

Method B: *n*-BuLi (2.0M in cyclohexane) was added dropwise to TMP (0.40 g, 2.53 mmol) in THF (4 mL) at −78 °C and stirred at RT for 1 hour. After this time the mixture was again cooled to −78 °C and 2,6-bis(tosyloxymethyl)pyridine (0.51 g, 1.14 mmol) was added dropwise. The mixture was then allowed to warm to RT and stirred for 16 hours. After this time the mixture was evaporated to dryness, washed with MeOH (3 × 10 mL) and dried *in vacuo*. Yield = 0.27 g (57%).

^1H NMR (400 MHz, $CDCl_3$): δ 7.45 (1H, t, $^3J_{HH}$ = 7.7 Hz, Ar*H*), 7.21 (2H, d, $^3J_{HH}$ = 7.7 Hz, Ar*H*), 2.99 (4H, d, $^2J_{CP}$ = 2.8 Hz, C*H*$_2$P), 1.65 – 1.37 (12H, m, C*H*$_2$), 1.14 (12H, d, $^3J_{HP}$ = 6.2 Hz, C*H*$_3$) and 0.97 ppm (12H, d, $^3J_{HP}$ = 17.5 Hz, C*H*$_3$). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 17.4 ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 160.4 (d, $^2J_{CP}$ = 12.0 Hz, ArC_q),

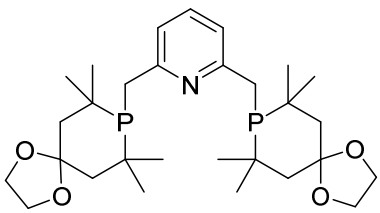
136.2 (s, Ar*C*), 120.9 (dd, $^{3}J_{CP}$ = 9.5 Hz, $^{5}J_{CP}$ = 1.3 Hz, Ar*C*), 40.4 (br. s, C*C*H$_2$), 31.2 (d, $^{2}J_{CP}$ = 27.8 Hz, *C*H$_3$), 30.9 (d, $^{1}J_{CP}$ = 25.6 Hz, *C*H$_2$P) 29.8 (d, $^{1}J_{CP}$ = 16.3 Hz, *C*(CH$_3$)$_2$), 26.2 (br. s, *C*H$_3$) and 20.4 ppm (d, $^{3}J_{CP}$ = 0.9 Hz, -*C*H$_2$-). HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 420.2949; found 420.2945. Elem. Anal. Calcd for $C_{25}H_{43}NP_2$: C, 71.57; H, 10.33; N, 3.34. Found: C, 68.82; H, 9.27; N, 3.19.

Example 16: Synthesis of *N*^{2},*N*^{6}-bis(2,2,6,6-tetramethylphosphinan-1-yl)pyridine-2,6-diamine, ^{TMP}(PN^{3}P)



NEt$_3$ (0.6 mL, 4.0 mmol) was added to 2,6-diaminopyridine (0.2 g, 1.9 mmol) in toluene (5 mL). The mixture was then cooled down to 0 °C and 1-chloro-2,2,6,6-tetramethylphosphinane was added (0.8 g, 4.0 mmol). *n*-BuLi (2.0 mL, 4.0 mmol) was added after the mixture was further cooled down to −78 °C. The mixture was heated to 80 °C and stirred for 16 hours. After that, the reaction mixture was filtered and the volatiles were removed in *vacuo*. It was then recrystallised with pentane at −40 °C to yield a white solid. Yield = 0.2 g (30 %). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.26 (1H, t, $^{3}J_{HH}$ = 8.0 Hz, C*H*), 6.49 (2H, d, $^{3}J_{HH}$ = 8.0 Hz, C*H*), 4.50 (2H, d, $^{2}J_{HP}$ = 11.1 Hz, N*H*), 1.57 (8H, m, C*H*$_2$), 1.44 (4H, m, C*H*$_2$), 1.15 (12H, d, $^{3}J_{HP}$ = 17.5 Hz, C*H*$_3$) and 1.01 ppm (12H, d, $^{3}J_{HP}$ = 11.1 Hz, C*H*$_3$). ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$): δ 159.9 (d, $^{2}J_{CP}$ = 20.9 Hz, Ar*C*), 139.0 (t, $^{4}J_{CP}$ = 2.1 Hz, Ar*C*), 98.6 (d, $^{3}J_{CP}$ = 19.6 Hz, Ar*C*), 36.1 (s, *C*H$_2$), 31.5 (d, $^{1}J_{CP}$ = 13.1 Hz, *C*$_q$), 28.9 (d, $^{2}J_{CP}$ = 8.1 Hz, *C*H$_3$), 26.8 (d, $^{2}J_{CP}$ = 31.0 Hz, *C*H$_3$) and 20.0 ppm (s, *C*H$_2$). ^{31}P{^{1}H} NMR (162 MHz, CDCl$_3$): δ 42.3 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 422.2854; found 422.2854. Elem. Anal. Calcd for $C_{23}H_{41}N_3P_2$: C, 65.53; H, 9.80; N, 9.97. Found: C, 65.38; H, 9.58; N, 9.86.

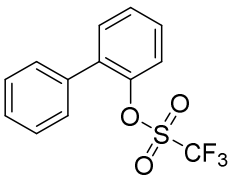
Example 17: Synthesis of 2,6-bis((7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decan-8-yl)methyl)pyridine, ^{TMPA}(PNP)



n-BuLi (3.7 mL, 6.6 mmol) was added dropwise to 4,4-(ethylenedioxy)-2,2,6,6-tetramethylphosphinane-borane (1.5 g, 6.6 mmol) in THF (15 mL) at −78 °C. The mixture was then warmed to room temperature and stirred for 1 hour. After that, 2,6-bis(chloromethyl)pyridine (0.5 g, 3.0 mmol) was added dropwise to the mixture at −78 °C and stirred at room temperature for 16 hours. The volatiles was removed *in vacuo*. Pyrrolidine (15 mL) was added, and the mixture was heated at 55 °C for 16 hours. The reaction mixture was cooled down, the volatiles were removed *in vacuo* and the crude material was washed with MeOH (3 × 10 mL) to yield a white solid. Yield = 1.4 g (86 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (1H, t, $^{3}J_{HH}$ = 7.7 Hz, C*H*), 7.19 (2H, d, $^{3}J_{HH}$ = 7.7 Hz, C*H*), 3.91 (8H, m, OCH_2), 2.99 (4H, d, $^{2}J_{HP}$ = 3.0 Hz, CH_2), 1.68 (8H, m, CH_2), 1.22 (12H, d, $^{3}J_{HP}$ = 7.1 Hz, CH_3) and 1.06 ppm (12H, d, $^{3}J_{HP}$ = 17.3 Hz, CH_3). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 160.3 (d, $^{2}J_{CP}$ = 12.4 Hz, ArC_q), 136.3 (s, Ar*C*), 120.9 (dd, $^{3}J_{CP}$ = 8.0 Hz, $^{5}J_{CP}$ = 1.3 Hz, Ar*C*), 110.3 (s, O_2C_q), 64.0 (d, $^{5}J_{CP}$ = 16.9 Hz, *C*H_2O), 46.2 (d, $^{2}J_{CP}$ = 3.4 Hz, C*C*H_2), 31.4 (d, $^{1}J_{CP}$ = 26.6 Hz, *C*$(CH_3)_2$). 31.1 (d, $^{2}J_{CP}$ = 16.6 Hz, *C*H_3), 30.7 (d, $^{1}J_{CP}$ = 25.4 Hz, *C*H_2P) and 27.4 ppm (s, *C*H_3). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 13.0 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 536.3059; found 536.3056. Elem. Anal. Calcd for $C_{29}H_{47}NO_4P_2$: C, 65.03; H, 8.84; N, 2.61. Found: C, 64.85; H, 8.52; N, 2.91.

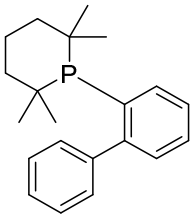
Example 18: Synthesis of 1-([1,1'-biphenyl]-2-yl)-2,2,6,6-tetramethylphosphinane

Synthesis of [1,1'-biphenyl]-2-yl trifluoromethanesulfonate



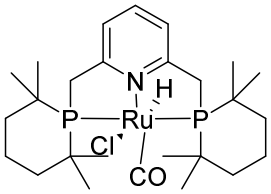
2-Phenylphenol (3.0 g, 17.6 mmol) was weighed and dissolved in CH_2Cl_2 (150 mL). Pyridine (4.2 g, 52.9 mmol) was added into the reaction mixture. The mixture was cooled to 0°C and trifluoromethylsulfonic anhydride (9.9 g, 35.2 mmol) was added dropwise. After the addition the mixture was allowed to warm to RT and stirred for 16 hours. Dilute HCl (2.0M aq) (150 mL), followed by extraction with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with deionised water (100 mL) and brine solution (100 mL) to give a clear dark brown solution. The organic phase was dried over $MgSO_4$ and solvent was removed *in vacuo* to yield a dark brown oil. The crude product was purified *via* column chromatography. Yield = 5.7 g (*quantitative*). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.56 ppm (9H, m, ArH). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 147.0

(Ar*C*O-) 135.7 (s, Ar*C*), 132.1 (s, Ar*C*), 129.5 (s, Ar*C*), 129.1 (s, Ar*C*), 128.7 (s, Ar*C*), 128.6 (s, Ar*C*), 128. (s, Ar*C*) and 122.2 (s, Ar*C*) and 118.5 ppm (q, $^{1}J_{CF}$ = 320.5 Hz *C*F_3). HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 303.0303; found 303.0297.



TMP (0.37 g, 2.23 mmol), [1,1'-biphenyl]-2-yl trifluoromethanesulfonate (0.50 g, 1.65 mmol), DBU (0.50 g, 3.31 mmol), $Pd(OAc)_2$ (2.0 mg, 0.01 mmol) were weighed and dissolved in toluene (5 mL) and heated at 110 °C for 16 hours. Toluene (5 mL) was added to the resulting solution, and it was washed three times with degassed DI water and dried over $MgSO_4$. The filtrate was evacuated to dryness *in vacuo* to give a yellow semi-solid. The crude product was recrystallized from MeOH at −20 °C (freezer) over 1 hour. The resulting crystals were dried *in vacuo. Yield* = 0.22 g (43%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (1H, dt, $^{3}J_{HH}$ = 7.4 Hz, $^{4}J_{HP}$ = 1.6 Hz, Ar*H*), 7.38 – 7.19 (8H, m, ArH), 1.95 – 1.82 (2H, m, C_qCH_2), 1.77 – 1.64 (2H, m, -$CH_2CH_2CH_2$-), 1.48 – 1.37 (2H, m, C_qCH_2), 1.11 (6H, d, CH_3, $^{3}J_{PH}$ = 19.2 Hz) and 0.87 ppm (6H, d, $^{3}J_{PH}$ = 9.4 Hz, CH_3). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 151.9 (d, $^{2}J_{CP}$ = 33.9 Hz, ArC_q), 144.0 (d, $^{3}J_{CP}$ = 7.9 Hz, ArC_q), 136.0 (d, $^{1}J_{CP}$ = 31.4 Hz, ArC_q), 134.9 (d, $^{3}J_{CP}$ = 4.2 Hz, Ar*C*H), 130.9 (d, $^{2}J_{CP}$ = 4.2 Hz, Ar*C*H), 130.8 (d, $^{3}J_{CP}$ = 5.1 Hz, Ar*C*H), 128.3 (s, Ar*C*H), 127.3 (s, Ar*C*H), 126.5 (s, Ar*C*H), 126.1 (s, Ar*C*H), 37.9 (s, C_qCH_2), 31.3 (d, $^{2}J_{CP}$ = 35.7 Hz, CH_3), 30.3 (d, $^{2}J_{CP}$ = 6.3 Hz, CH_3), 30.0 (d, $^{1}J_{CP}$ = 18.4 Hz, $C(CH_3)_2$) and 20.4 ppm (s, -CH_2-). $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ −2.4 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 311.1929; found 311.1922. Elem. Anal. Calcd for $C_{21}H_{27}P$: C, 81.25; H, 8.77. Found: C, 80.31; H, 8.27.

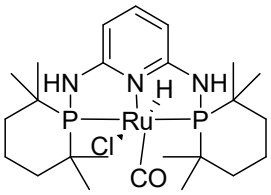
Example 19: Synthesis of [^{TMP}(PN^{3}P)Ru(CO)(Cl)H]



Carbonylchlorohydridotris(triphenylphosphine)ruthenium(II) (221 mg, 0.23 mmol) and ^{TMP}(PNP) ligand (120 mg, 0.29 mmol) were stirred at 65 °C for 16 hours. It was then

cooled to RT and reduced in volume to approximately 1 mL. Diethyl ether (5 mL) was added to precipitate a pale yellow solid which was filtered, washed with more diethyl ether (2 × 5 mL) and dried *in vacuo*. Yield = 0.11 g (81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (1H, t, $^{3}J_{HH}$ = 7.7 Hz, Ar*H*), 1.14 (2H, d, $^{3}J_{HH}$ = 7.7 Hz, Ar*H*), 3.98 (2H, dt, $^{2}J_{HH}$ = 16.5 Hz, $|^{2}J_{HP} + {}^{4}J_{HP}|$ = 3.4 Hz, C*H*$_2$P), 3.47 (2H, dt, $^{2}J_{HH}$ = 16.5 Hz, $|^{2}J_{HP} + {}^{4}J_{HP}|$ = 3.6 Hz, C*H*$_2$P), 1.82 – 1.53 (12H, m, C*H*$_2$), 1.59 (6H, t, $|^{3}J_{HP} + {}^{5}J_{HP}|$ = 8.2 Hz, C*H*$_3$), 1.48 (6H, $|^{3}J_{HP} + {}^{5}J_{HP}|$ = 6.7 Hz, C*H*$_3$), 1.39 (6H, $|^{3}J_{HP} + {}^{5}J_{HP}|$ = 7.8 Hz, C*H*$_3$), 0.84 (6H, $|^{3}J_{HP} + {}^{5}J_{HP}|$ = 6.6 Hz, C*H*$_3$) and −15.1 ppm (1H, t, $^{2}J_{HP}$ = 19.2 Hz, Ru-*H*). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 209.0 (t, $^{2}J_{CP}$ = 11.7 Hz, *C*=O), 163.6 (t, $^{2}J_{CP}$ = 5.2 Hz, Ar*C*$_q$), 137.0 (s, Ar*C*), 119.8 (t, $^{3}J_{CP}$ = 4.5 Hz, Ar*C*), 40.7 (s, C_qCH_2), 38.3 (s, C_qCH_2), 37.0 (t, $^{1}J_{CP}$ = 6.6 Hz, C*H*$_2$P), 36.1 (t, $^{1}J_{CP}$ = 7.3 Hz, *C*$(CH_3)_2$), 33.6 (t, $^{1}J_{CP}$ = 11.0 Hz, *C*$(CH_3)_2$), 30.7 (s, *C*H_3), 29.9 (s, *C*H_3), 27.4 (t, $^{2}J_{CP}$ = 7.2 Hz, *C*H_3), 27.0 (t, $^{2}J_{CP}$ = 6.4 Hz, *C*H_3) and 19.6 ppm (s, -*C*H_2-). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 70.6 ppm. HR-MS (+ve ESI): m/z (*calc.*) $[M-Cl]^+$ 550.1942; found 550.1944. Elem. Anal. Calcd for $C_{26}H_{44}ClNOP_2Ru$: C, 53.37; H, 7.58; N, 2.39. Found: C, 51.85; H, 7.085; N, 1.93.

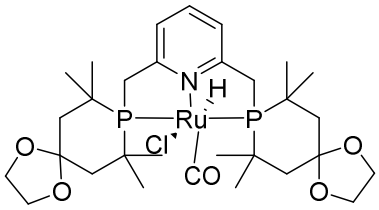
Example 20: Synthesis of [^{TMP}(PN^{3}P)Ru(CO)(Cl)H]



Carbonylchlorohydridotris(triphenylphosphine)ruthenium(II) (271 mg, 0.29 mmol) and ^{TMP}(PN^{3}P) ligand (150 mg, 0.36 mmol) were heated at 65 °C in THF (5 mL) for 16 hours. After cooling the white precipitate was filtered, washed with diethyl ether (2 × 5 mL) and dried *in vacuo*. Yield = 94 mg (56%). ^{1}H NMR (400 MHz, CD_3CN): δ 8.52 (2H, s, N*H*), 7.16 (1H, t, $^{3}J_{HH}$ = 8.0 Hz, Ar*H*), 6.72 (2H, t, $^{3}J_{HH}$ = 8.0 Hz, Ar*H*), 2.41 (2H, t, $^{3}J_{HH}$ = 11.4 Hz, C*H*$_2$), 2.18 (2H, t, $^{3}J_{HH}$ = 11.6 Hz, C*H*$_2$), 1.77 (2H, q, $^{3}J_{HH}$ = 12.8 Hz, C*H*$_2$), 1.69 – 1.57 (6H, m, C*H*$_2$), 1.51 (6H, t, $|^{2}J_{HP} + {}^{4}J_{HP}|$ = 9.5 Hz, C*H*$_3$), 1.28 (6H, t, $|^{2}J_{HP} + {}^{4}J_{HP}|$ = 9.2 Hz, C*H*$_3$), 1.23 (6H, t, $|^{2}J_{HP} + {}^{4}J_{HP}|$ = 7.0 Hz, C*H*$_3$), 1.27 (6H, t, $|^{2}J_{HP} + {}^{4}J_{HP}|$ = 7.2 Hz, C*H*$_3$), and −14.4 ppm (1H, t, $^{2}J_{HP}$ = 20.0 Hz, Ru-*H*). ^{13}C{^{1}H} NMR (101 MHz, CD_3CN): δ 206.8 (t, $^{2}J_{CP}$ = 10.2 Hz, Ru-*C*=O), 162.5 (t, $^{2}J_{CP}$ = 7.1 Hz, Ar*C*$_q$), 140.2 (s, Ar*C*), 99.4 (t, $^{3}J_{CP}$ = Hz, Ar*C*), 39.7 (s , C_qCH_2), 37.7 (s, C_qCH_2), 37.7 (t, $|^{1}J_{CP} + {}^{3}J_{CP}|$ = 11.9 Hz, *C*$(CH_3)_2$), 37.4 (t, $|^{1}J_{CP} + {}^{3}J_{CP}|$ = 9.7 Hz, *C*$(CH_3)_2$), 29.3 (s, *C*H_3), 29.0 (s, *C*H_3) 27.2 (t, $^{2}J_{CP}$ = 10.1 Hz, *C*H_3), 25.8 (t, $^{2}J_{CP}$ = 8.4 Hz, *C*H_3) and 19.9 ppm (s, -*C*H_2-).

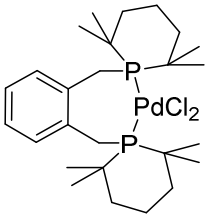
$^{31}P\{^{1}H\}$ NMR (162 MHz, CD_3CN): δ 123.8 ppm. Elem. Anal. Calcd for $C_{24}H_{42}ClN_3OP_2Ru$: C, 49.10; H, 7.21; N, 7.16. Found: C, 48.06; H, 7.15; N, 6.72.

Example 21: Synthesis of [^{TMPA}(PNP)Ru(CO)(Cl)H]



Carbonylchlorohydridotris(triphenylphosphine)ruthenium(II) (0.71 g, 0.74 mmol) and ^{TMPA}(PNP) ligand (0.50 g, 0.93 mmol) were heated at 60 °C in THF (12 mL) for 16 hours. After cooling a white precipitate was observed which was filtered, washed with diethyl ether (2 × 12 mL) and dried *in vacuo*. Yield = 0.42 g (80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (1H, t, $^{3}J_{HH}$ = 7.7 Hz, Ar*H*), 7.14 (2H, d, $^{3}J_{HH}$ = 7.8 Hz, Ar*H*), 4.08 – 4.00 (4H, m, C*H*$_2$O), 3.99 (2H, dt, $^{2}J_{HH}$ = 16.7 Hz, $|^{2}J_{HP} + {}^{4}J_{HP}|$ = 3.3 Hz, C*H*$_2$P,), 3.93 – 3.85 (4H, m, C*H*$_2$O), 3.45 (2H, dt, $^{2}J_{HH}$ = 16.7, $|^{2}J_{HP} + {}^{4}J_{HP}|$ = 3.6 Hz, C*H*$_2$P), 1.99 – 1.75 (8H, m, CC*H*$_2$), 1.72 (6H, t, $|^{3}J_{HP} + {}^{5}J_{HP}|$ = 8.4 Hz, C*H*$_3$), 1.53 (6H, $|^{3}J_{HP} + {}^{5}J_{HP}|$ = 6.6 Hz, C*H*$_3$), 1.52 (6H, $|^{3}J_{HP} + {}^{5}J_{HP}|$ = 8.1 Hz, C*H*$_3$) and 0.89 ppm (6H, $|^{3}J_{HP} + {}^{5}J_{HP}|$ = 6.6 Hz, C*H*$_3$). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 208.3 (t, $^{2}J_{CP}$ = 11.7 Hz, Ru-*C*=O), 163.3 (t, $^{2}J_{CP}$ = 5.2 Hz, Ar*C*$_q$), 137.2 (s, Ar*C*), 119.9 (t, $^{3}J_{CP}$ = 4.5 Hz, Ar*C*), 108.8 (s, O_2C_q), 65.3 (s, *C*H$_2$O), 63.2 (s, *C*H$_2$O), 46.8 (s, C_qCH_2), 44.7 (s, C_qCH_2), 37.2 (t, $^{1}J_{CP}$ = 6.5 Hz, *C*H$_2$P), 36.9 (t, $^{1}J_{CP}$ = 7.4 Hz, *C*(CH$_3$)$_2$), 34.4 (t, ^{1}J = 11.0 Hz, *C*(CH$_3$)$_2$), 31.1 (s, *C*H$_3$), 30.4 (s, *C*H$_3$), 28.2 (t, $^{2}J_{CP}$ = 7.2 Hz, *C*H$_3$) and 27.7 ppm (t, $^{2}J_{CP}$ = 6.4 Hz, *C*H$_3$). $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 67.3 ppm. HR-MS (+ve ESI): m/z (calc.) $[M-Cl]^+$ 666.2051; found 666.2057. Elem. Anal. Calcd for $C_{30}H_{48}ClNO_5P_2Ru$: C, 51.39; H, 6.90; N, 2.00. Found: C, 51.05; H, 7.07; N, 1.86.

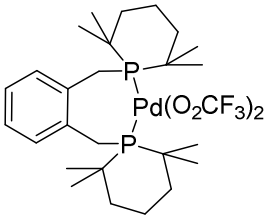
Example 22: Synthesis of [(BTMPX)$PdCl_2$]



BTMPX (0.20 g, 0.50 mmol) and [Pd(dba)$_2$] (0.27 g, 0.50 mmol) were mixed together in CH_2Cl_2 (5 mL). After 90 minutes HCl (2.0M in Et_2O, 0.5 mL) was added and air was

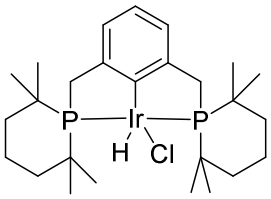
introduced into the reaction flask. After stirring for 16 hours the mixture was passed through a glass filter and reduced in volume to ~3mL. Et_2O (10 mL) was added which precipitated a yellow solid which was filtered and washed with Et_2O (2 × 10 mL) and then dried *in vacuo*. Yield = 1.30 g (44%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 – 7.16 (2H, m, Ar*H*), 7.16 – 6.72 (2H, m, Ar*H*), 3.89 – 3.05 (4H, m, C*H*$_2$), 3.35 –2.38 (4H, m, C*H*$_2$), 2.31 – 0.06 ppm (24H, m). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 133.9 (br. s, Ar*C*$_q$), 133.3 (br. s, Ar*C*H), 127.6 (br. s, Ar*C*H), 40.4 (br. s, *C*H_2CH$_2$*C*H_2), 37.6 (br. s, *C*$(CH_3)_2$), 33.3 (br. s, *C*H_3), 29.4 (br. s, *C*H_3) and 19.5 ppm (br. s, CH_2*C*H_2CH$_2$). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ br s 28.4 ppm. Elem. Anal. Calcd for $C_{26}H_{44}Cl_2P_2Pd$: C, 52.41; H, 7.44. Found: C, 51.32; H, 7.30.

Example 23: Synthesis of [(BTMPX)Pd$(O_2CCF_3)_2$]



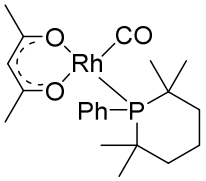
[(BTMPX)$PdCl_2$] (0.10 g, 0.17 mmol) was dissolved in CH_2Cl_2 (5 mL) to give a clear deep orange solution. To this was added [Ag$(O_2CCF_3)_2$] (0.089 g, 0.41 mmol) which gave a yellow solution. After 16 hours the mixture was passed through a glass filter and reduced in volume to ~1mL. Pentane (3 mL) was added which precipitated a yellow powder which was dried *in vacuo*. Single crystals suitable for X-ray diffraction were grown *via* a vapour diffusion of pentane into a saturated solution of the compound in CH_2Cl_2. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 – 7.40 (2H, m, Ar*H*), 7.40 – 7.20 (2H, m, Ar*H*), 3.24 (4H, d, $^2J_{HP}$ = 12.1 Hz, C*H*$_2$P), 2.35 (4H, m, C*H*$_2$) and 1.94 – 1.06 ppm (32H, m). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 162.2 (q, $^2J_{CF}$ = 36.36 Hz, *C*O_2CF_3), 128.2 (s, ArC*H*), 115.9 (q, $^1J_{CP}$ = 291.3 Hz, *C*F_3), 38.7 (s, C_q*C*H_2), 37.0 (d, $^1J_{CP}$ = 17.2 Hz, *C*$(CH_3)_2$), 32.3 (br. s, *C*H_3), 27.9 (s, *C*H_3), 27.5 (d, $^1J_{CP}$ = 18.0 Hz, *C*H_2P) and 19.0 ppm (br. s, CH_2*C*H_2CH$_2$). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 32.3 ppm. ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$): δ −75.5 ppm (s, C*F*$_3$).

Example 24: Synthesis of [TMP(PCP)Ir(H)Cl]



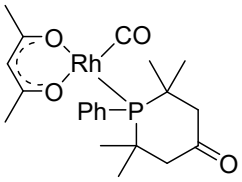
^{TMP}(PCP) (60 mg, 0.14 mmol) and [(COD)IrCl]$_2$ (43.7 mg, 0.065 mmol) were dissolved in toluene (2 mL) and heated to 120 °C giving a deep red solution. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.95 (2H, d, $^3J_{HH}$ = 6.9 Hz, ArC*H*), 6.74 (1H, t, $^3J_{HH}$ = 7.6 Hz, ArC*H*), 3.38 – 3.09 (4H, m, C*H*$_2$), 2.35 – 2.02 (4H, m, -*CH*$_2$-), *1*.89 – 1.43 (8H, m, C*H*$_2$) 1.39 – 1.31 (6H, m, C*H*$_3$), 1.30 – 1.16 (12H, m, C*H*$_3$), 1.15 – 1.07 (6H, m, C*H*$_3$), −40.44 ppm (1H, s, Ir-*H*). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 32.3 ppm.

Example 25: Synthesis of [(acac)Rh(CO)(Phenyl phosphinane)]



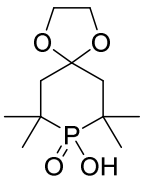
Phenyl phosphinane (0.10 g, 0.42 mmol), was dissolved in CH_2Cl_2 (5 mL). [(acac)Rh(CO)$_2$] (0.11 g, 0.42 mmol) was dissolved in CH_2Cl_2 (5 mL) and added. The mixture turned dark yellow after 30 mins and was evaporated to dryness. Pentane (2 mL) was added and the mixture was placed in the freezer (−20 °C) giving a yellow precipitate which was filtered and dried *in vacuo*. Yield = 0.14 g (71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (2H, br s. Ar*H*), 7.41 – 7.33 (3H, m, Ar*H*), 5.49 (1H, s, C*H*(acac), 2.09 (3H, s, C*H*$_3$ (acac)), 2.07 – 1.59 (6H, m, C*H*$_2$), 1.77 (3H, s, C*H*$_3$ (acac)), 1.64 (6H, d, $^3J_{HP}$ = 16.4 Hz, C(C*H*$_3$)$_2$) and 1.02 ppm (6H, d, $^3J_{HP}$ = 13.7 Hz, C(C*H*$_3$)$_2$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 190.9 (dd, $^1J_{RhC}$ = 75.7 Hz, $^2J_{CP}$ = 22.6 Hz, Rh-*C*=O), 188.0 (s, acac *C*=O), 184.8 (s, acac *C*=O), 137.0 (br s., Ar*C*), 134.2 (d, $^1J_{CP}$ = 34.5 Hz, Ar*C*$_q$), 129.9 (d, $^3J_{CP}$ = 2.3 Hz, Ar*C*), 127.3 (d, $^2J_{CP}$ = 9.6 Hz, Ar*C*), 101.0 (d, $^3J_{RhC}$ = 2.4 Hz, acac *C*H), 39.6 (d, $^2J_{CP}$ = 2.7 Hz, *C*H$_2$), 34.0 (dd, $^1J_{CP}$ = 20.7 Hz, $^2J_{CRh}$ = 0.6 Hz, *C*(CH$_3$)$_2$), 29.9 (d, $^2J_{CP}$ = 11.4 Hz, C(*C*H$_3$)$_2$), 29.4 (s, C(*C*H$_3$)$_2$), 27.8 (dd, $^3J_{CRh}$ = 5.1 Hz, $^4J_{CP}$ = 1.0 Hz, acac *C*H$_3$), 26.8 (s, acac *C*H$_3$) and 19.4 ppm (d, $^3J_{CP}$ = 4.1 Hz, CH$_2$*C*H$_2$CH$_2$). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 71.1 ppm (d, $^1J_{RhP}$ = 180.0 Hz). IR (CH_2Cl_2): $\tilde{\nu}$ 1964 (s) C=O str.

Example 26: Synthesis of [(acac)Rh(CO)(Phenyl phosphorinone)]



Phenyl phosphorinone (0.1 g, 0.40 mmol), was dissolved in CH_2Cl_2 (5 mL). [(acac)Rh(CO)$_2$] (0.11 g, 0.40 mmol) was dissolved in CH_2Cl_2 (5 mL) and added. The mixture turned dark yellow after 30 mins and was reduced in volume to ~5mL. Pentane (12 mL) was added and the mixture was passed through a glass filter. The orange solution was evaporated to dryness giving a light brown powder. Yield = 0.11 g (56 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 – 8.27 (2H, m, Ar*H*), 7.49 – 7.40 (3H, m, Ar*H*), 5.53 (1H, s, acac C*H*), 2.83 (2H, d, $^3J_{HP}$ = 3.7 Hz, C*H*$_2$), 2.80 (2H, br. s., C*H*$_2$), 2.10 (3H, s, acac C*H*$_3$), 1.83 (3H, s, acac C*H*$_3$), 1.70 (6H, d, $^3J_{HP}$ = 16.1 Hz, C(C*H*$_3$)$_2$), and 1.21 ppm (6H, d, $^3J_{HP}$ = 12.4 Hz, C(C*H*$_3$)$_2$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 208.8 (d, $^3J_{CP}$ = 4.2 Hz, *C*=O), 189.6 (dd, $^1J_{RhC}$ = 75.3 Hz, $^2J_{CP}$ = 23.3 Hz, Rh-*C*=O), 188.3 (s, acac *C*=O), 184.7 (s, acac *C*=O), 135.9 (d, $^2J_{CP}$ = 11.0 Hz, Ar*C*H), 132.8 (d, $^1J_{CP}$ = 38.0 Hz, Ar*C*$_q$), 130.7 (d, $^4J_{CP}$ = 2.3 Hz, Ar*C*H) 128.0 (d, $^3J_{CP}$ = 9.7 Hz, Ar*C*H), 101.2 (d, $^3J_{RhC}$ = 2.4 Hz, acac *C*H), 54.8 (d, $^2J_{CP}$ = 1.3 Hz, *C*H$_2$), 37.9 (dd, $^1J_{CP}$ = 19.7 Hz, $^2J_{CRh}$ = 0.8 Hz, *C*(CH$_3$)$_2$), 31.4 (d, $^2J_{CP}$ = 10.1 Hz, C(*C*H$_3$)$_2$), 28.5 (s, C(*C*H$_3$)$_2$), 27.8 (dd, $^3J_{RhC}$ = 5.3 Hz, $^4J_{CP}$ = 0.9 Hz, acac *C*H$_3$) and 26.0 ppm (s, acac *C*H$_3$). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 69.0 ppm (d, $^1J_{RhP}$ = 182.9 Hz). IR (CH_2Cl_2): $\tilde{\nu}$ 1964 (s) C=O str.

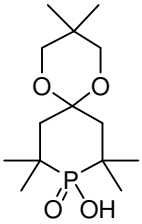
Example 27: Synthesis of 4,4-(ethylenedioxy)-2,2,6,6-tetramethylphosphaninic acid



2,2,6,6-Tetramethylphosphorinic acid (1.0 g, 5.0 mmol) and ethylene glycol (8.0 mL) were dissolved in toluene (50 mL) and a catalytic amount of *p*-toluene sulfonic acid (93 mg, 0.5 mmol) was added. The mixture was then heated to 150 °C using a dean & stark apparatus to remove H_2O. After 16 hours the mixture was cooled, then washed with DI H_2O (2 × 50 mL) and brine (50 mL), dried over anhydrous magnesium sulfate and evaporated to yield a white solid. Yield = 0.7 g (56 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.91 (4H, s, OC*H*$_2$), 1.87 (4H, d, $^3J_{HP}$ = 15.3 Hz, C*H*$_2$) and 1.29 ppm (12H, d, $^3J_{HP}$ = 13.8 Hz, C*H*$_3$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 108.4 (d, $^3J_{CP}$ = 7.9 Hz, *C*$_q$), 64.0 (s, *C*H$_2$O),

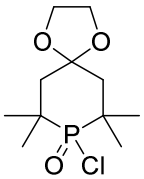
46.4 (s, *C*H_2), 33.2 (d, $^1J_{CP}$ = 84.7 Hz, C_q) and 24.4 ppm (d, $^2J_{CP}$ = 1.1 Hz, *C*H_3). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 61.5 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 249.1256; found 249.1251. Elem. Anal. Calcd for $C_9H_{17}O_3P$: C, 53.22; H, 8.53. Found: C, 53.29; H, 16.78.

Example 28: Synthesis of 9-hydroxy-3,3,8,8,10,10-hexamethyl-1,5-dioxa-9-phosphaspiro[5.5]undecane 9-oxide



2,2,6,6-Tetramethylphosphorinic acid (0.20 g, 0.98 mmol) and neopentyl glycol (0.61 g, 5.88 mmol) were dissolved in toluene (80 mL) and a catalytic amount of *p*-toluenesulfonic acid (18.6 mg, 0.098 mmol) was added. The mixture was heated to 140 °C using a dean & stark apparatus to remove H_2O. After 72 hours the mixture was cooled and an additional equivalent of neopentyl glycol was added (0.10 g, 0.98 mmol). The mixture was then heated again for a further 16 hours. After cooling the mixture was washed with DI H_2O (2 × 40 mL) and brine (40 mL). The organic phase was then dried over $MgSO_4$ and then evaporated to give a white solid. Yield = 0.15 g (52.8 %). ^1H NMR (400 MHz, $CDCl_3$): δ 9.24 (1H, br s, O*H*), 3.45 (4H, s, C*H*$_2$O), 2.00 (4H, d, $^3J_{HP}$ = 15.5 Hz, CC*H*$_2$), 1.27 (12H, d, $^3J_{HP}$ = 13.7 Hz, C*H*$_3$) and 0.94 ppm (6H, s, C*H*$_3$). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 62.4 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 291.1725; found 291.1721.

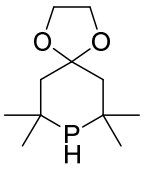
Example 29: Synthesis of 8-chloro-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane 8-oxide



4,4-(Ethylenedioxy)-2,2,6,6-tetramethylphosphaninic acid (4.8 g, 19.2 mmol) was dissolved in CH_2Cl_2 (100 mL), then lutidine (5.2 g, 5.6 mL, 48.1 mmol) and DMF (0.14 g, 0.15 mL, 0.19 mmol) were added. The mixture was cooled to 0 °C, whereupon oxalyl chloride (12.2 g, 8.1 mL, 96.2 mmol) was added. A gas was evolved and there was a

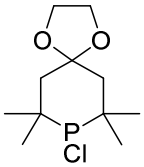
colour change from yellow to orange. After 72 hours the volatiles were removed *in vacuo* and the crude material was extracted with pentane (3 × 20 mL) filtered and evaporated to give an off white solid. Yield = 3.5 g (72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.02 – 3.86 (4H, m, OC*H*$_2$), 2.10 – 1.82 (4H, m, C*H*$_2$), 1.52 (6H, d, $^{3}J_{PH}$ = 15.7 Hz, C*H*$_3$) and 1.38 ppm (6H, d, $^{3}J_{PH}$ = 16.5 Hz, C*H*$_3$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 107.5 (d, $^{3}J_{CP}$ = 7.5 Hz, O$_2$*C*$_q$), 64.8 (s, O*C*H$_2$), 63.8 (s, O*C*H$_2$), 46.4 (d, $^{2}J_{CP}$ = 1.2 Hz, *C*H$_2$), 39.1 (d, $^{1}J_{CP}$ = 62.2 Hz, *C*$_q$), 26.7 (d, $^{2}J_{CP}$ = 3.4 Hz, *C*H$_3$) and 24.1 ppm (s, *C*H$_3$). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 85.9 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 267.0917; found 267.0906.

Example 30: Synthesis of 7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane (TMPA)



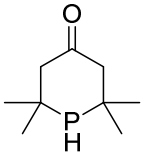
8-Chloro-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane 8-oxide (3.5 g, 13.9 mmol) in Et_2O (20 mL) was added dropwise over 15 minutes to a suspension of $LiAlH_4$ (1.3 g, 33.4 mmol) in Et_2O (100 mL) which had been cooled to 0 °C. The mixture was allowed to warm to RT and stirred for 72 hours. After this time the mixture was cooled in ice and the excess $LiAlH_4$ was quenched with NaOH (aq, 20%, 2.5 mL), followed by DI H_2O (2.5 mL). It was warmed to RT and drying agent ($MgSO_4$) was added and the mixture filtered. The volatiles were removed *in vacuo* to give a white solid. Yield = 1.8 g (56%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.00 – 3.85 (4H, m, OC*H*$_2$), 2.68 (1H, d of sept, $^{1}J_{HP}$ = 198.8 Hz, $^{3}J_{HH}$ = 1.6 Hz, P*H*), 1.85 (2H, dd, $^{1}J_{HH}$ = 13.6 Hz, $^{3}J_{HP}$ = 4.4 Hz, C*H*), 1.49 (2H, d, $^{1}J_{HH}$ = 13.6 Hz, C*H*), 1.26 (6H, d, $^{3}J_{HP}$ = 14.4 Hz, C*H*$_3$) and 1.09 ppm (6H, d, $^{3}J_{HP}$ = 14.1 Hz, C*H*$_3$). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ −16.2 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 217.1357; found 217.1348. Elem. Anal. Calcd for $C_{11}H_{21}O_2P$: C, 61.09; H, 9.79. Found: C, 61.34; H, 9.68.

Example 31: Synthesis of 8-Chloro-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane, TMPA-Cl



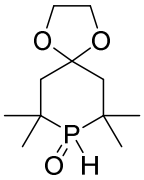
TMPA (0.20 g, 0.92 mmol) was dissolved in THF (2 mL). C_2Cl_6 (0.22 g, 0.92 mmol) in THF (2 mL) was added. The mixture was stirred for 3 weeks and then the volatiles were removed *in vacuo*. Yield = 0.12 g (52%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.98 (2H, dt, $^3J_{HH}$ = 6.5 Hz, J = 0.7 Hz, C*H*$_2$O), 3.88 (2H, dt, $^3J_{HH}$ = 6.8 Hz, J = 0.7 Hz, C*H*$_2$O), 1.95 (2H, d, $^2J_{HH}$ = 14.2 Hz, C*H*$_2$), 1.52 (2H, dd, $^2J_{HH}$ = 14.1 Hz, $^3J_{HP}$ = 6.2 Hz, C*H*$_2$), 1.33 (6H, d, $^3J_{HP}$ = 18.5 Hz, C*H*$_3$) and 1.20 ppm (6H, d, $^3J_{HP}$ = 12.3 Hz, C*H*$_3$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 110.2 (s, O_2C_q), 65.1 (s, *C*H$_2$O), 63.1 (s, *C*H$_2$O), 40.9 (d, $^2J_{CP}$ = 2.9 Hz, C_qCH_2), 35.1 (d, $^1J_{CP}$ = 33.4 Hz, *C*(CH$_3$)$_2$), 31.2 (d, $^2J_{CP}$ = 11.6 Hz, *C*H$_3$) and 25.4 ppm (d, $^2J_{CP}$ = 34.7 Hz, *C*H$_3$). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 120.7 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 251.0968; found 251.0960.

Example 32: Synthesis of 2,2,6,6-tetramethylphosphinan-4-one, TMPK



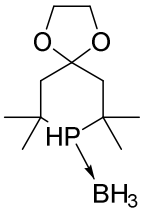
TMPA (0.97 g, 4.49 mmol) was dissolved in THF (5 mL) and degassed 3.0 M HCl (aq) was added. The mixture was stirred for 16 hours. After this time degassed DI H_2O (30 mL) was added and then the product was extracted with Et_2O (3 × 20 mL), dried over $MgSO_4$ and evaporated to give a colourless oil. Yield = 0.55 g (69%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.19 (1H, d, $^1J_{PH}$ = 198.1 Hz, P*H*), 2.49 (2H, d, $^2J_{HH}$ = 11.8 Hz, C*H*$_2$), 2.37 (2H, dd, $^2J_{HH}$ = 12.5 Hz, $^2J_{HP}$ = 3.3 Hz, C*H*$_2$) and 1.31 – 1.09 ppm (12H, m, C*H*$_3$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 211.6 (s, *C*=O), 57.6 (d, $^2J_{CP}$ = 6.3 Hz, *C*H$_2$), 33.6 (d, $^1J_{CP}$ = 12.4 Hz, *C*(CH$_3$)$_2$), 32.1 (d, $^2J_{CP}$ = 12.9 Hz, *C*H$_3$) and 27.5 ppm (d, $^2J_{CP}$ = 24.3 Hz, *C*H$_3$). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ −11.9 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 173.1095; found 173.1096.

Example 33: Synthesis of 7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane 8-oxide, TMPA=O.



TMPA (0.20 g, 0.92 mmol) was dissolved in CH_2Cl_2 (5 mL) and cooled to 0 °C. *m*-CPBA (70%, aq) (0.24 g, 0.97 mmol) in CH_2Cl_2 (3 mL) was added slowly. After 10 minutes the ice bath was removed and the mixture was allowed to warm to RT. The mixture was stirred for 2 hours and the volatiles were them removed *in vacuo*. The white solid was taken up CH_2Cl_2 (10 mL) and washed with saturated $NaHCO_3$ (2 × 10 mL), then the combined aqueous portion was then backwashed with CH_2Cl_2 (10 mL). The combined organic phases were washed with brine (10 mL) and dried over $MgSO_4$. Filtration and evaporation gave a white solid which was handled under argon. Yield = 0.12 g (56%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.30 (1H, d, $^1J_{HP}$ = 432.4 Hz, P*H*), 3.98 (2H, t, $^3J_{HH}$ = 6.4 Hz, *C*H_2O), 3.84 (2H, t, $^3J_{HH}$ = 6.6 Hz, *C*H_2O), 1.89 – 1.71 (4H, m, C_qCH_2), 1.38 (6H, d, $^3J_{HP}$ = 12.4 Hz, C*H*$_3$) and 1.27 ppm (6H, d, $^3J_{HP}$ = 15.8 Hz, C*H*$_3$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 107.6 (d, $^3J_{CP}$ = 6.5 Hz, O_2C_q), 65.0 (s, *C*H_2O), 63.5 (s, *C*H_2O), 45.7 (d, $^2J_{CP}$ = 2.4 Hz, *C*H_2), 32.8 (d, $^1J_{CP}$ = 59.4 Hz, *C*$(CH_3)_2$), 28.2 (d, $^2J_{CP}$ = 1.0 Hz, *C*H_3) and 20.8 ppm (s, *C*H_3). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 57.1 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 233.1307; found 233.1299. Elem. Anal. Calcd for $C_{11}H_{21}O_3P$: C, 56.89; H, 9.11. Found: C, 57.52; H, 8.94.

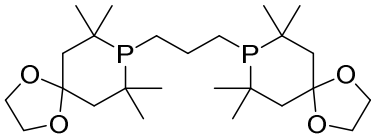
Example 34: Synthesis of 7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane borane complex.



TMPA (0.88 g, 3.82 mmol) was dissolved in THF (10 mL) and borane dimethyl sulfide complex (2.0M in THF, 2.01 mL, 4.0 mmol) was added. The mixture was stirred for 16 hours before being evaporated to give a white solid which was washed with pentane (2 x 10 mL) and dried *in vacuo*. Yield = 0.55 g (63%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.03 (1H, d of q, $^1J_{HP}$ = 346.7 Hz, $^3J_{HH}$ = 6.3 Hz, P*H*), 4.03 – 3.85 (4H, m, OC*H*$_2$), 1.91 (2H, dd, $^3J_{HP}$ = 17.2 Hz, $^2J_{HH}$ = 14.0 Hz, C*H*), 1.69 (2H, dd, $^2J_{HH}$ = 13.8 Hz, $^3J_{HP}$ = 2.2 Hz, C*H*), 1.33 (6H, d, $^3J_{HP}$ = 14.3 Hz, C*H*$_3$), 1.23 (6H, d, $^3J_{HP}$ = 15.4 Hz, C*H*$_3$) and 0.46 ppm

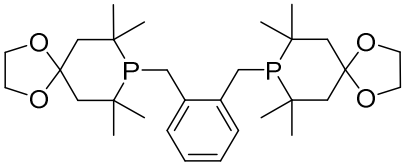
(3H, q, $^{1}J_{BH}$ = 99.2 Hz, B*H*$_3$). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 108.4 (d, $^{3}J_{CP}$ = 5.0 Hz, O*C*$_q$), 65.3 (s, O*C*H$_2$), 63.4 (s, O*C*H$_2$), 48.1 (d, $^{2}J_{CP}$ = 5.2 Hz, *C*H$_2$), 30.8 (d, $^{2}J_{CP}$ = 1.2 Hz, *C*H$_3$), 29.0 (d, $^{1}J_{CP}$ = 28.9 Hz, *C*$_q$) and 22.7 ppm (d, $^{2}J_{CP}$ = 7.5 Hz, *C*H$_3$). $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 31.3 ppm (q, $^{1}J_{PB}$ = 56.9 Hz). HR-MS (+ve ESI): m/z (calc.) [M+Na]+ 253.1505; found 253.1500. Elem. Anal. Calcd for $C_{11}H_{24}BO_2P$: C, 57.42; H, 10.51. Found: C, 57.19; H, 10.40.

Example 35: Synthesis of 1,3-bis(7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decan-8-yl)propane.



n-BuLi (2.0M in hexanes, 0.79 mL, 1.57 mmol) was added dropwise to TMPA (0.34 g, 1.57 mmol) in THF (5 mL) at −78 °C, the colour turned instantly yellow. It was allowed to warm to RT whereupon it became milky white in appearance. After stirring for 1 hour it was cooled to −78 °C and 1,3-dibromopropane (0.13 g, 0.63 mmol) in THF (0.5 mL) was added dropwise. It was warmed to RT giving a clear yellow solution. After 16 hours the volatiles were removed *in vacuo.* MeOH was added (4 mL) and the solution was placed in the freezer for 72 hours (−20 °C). The solid formed was filtered and dried. Yield = 0.09 g (31%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.91 (8H, s, OC*H*$_2$), 1.77 – 1.67 (2H, m, -C*H*$_2$-), 1.63 (8H, d, $^{3}J_{HP}$ = 8.0 Hz, C*H*$_2$), 1.53 – 1.48 (4H, m, C*H*$_2$), 1.20 (12H, d, $^{3}J_{HP}$ = 16.8 Hz, C*H*$_3$) and 1.12 ppm (12H, d, $^{3}J_{HP}$ = 7.7 Hz, C*H*$_3$). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 110.4 (s, O$_2$*C*$_q$), 64.0 (d, $^{5}J_{CP}$ = 15.3 Hz, O*C*H$_2$), 45.9 (s, *C*H$_2$), 31.5 (d,$^{2}J_{CP}$ = 26.4 Hz, *C*H$_3$), 30.4 (d, $^{1}J_{CP}$ = 14.9 Hz, *C*(CH$_3$)$_2$), 29.0 (t, $^{2}J_{CP}$ = 24.0 Hz, -*C*H$_2$-), 27.6 (s, *C*H$_3$) and 22.3 ppm (dd, $^{1}J_{CP}$ = 22.1 Hz, $^{3}J_{CP}$ = 13.1 Hz, P*C*H$_2$). $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 4.0 ppm.

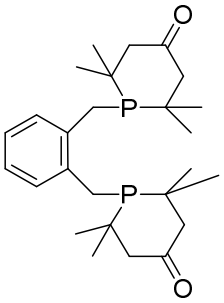
Example 36: Synthesis of 1,2-bis((7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decan-8-yl)methyl)benzene.



n-BuLi (2.0M in hexanes, 1.1 mL, 2.2 mmol) was added dropwise to 7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane borane complex (0.46 g, 1.99

mmol) in THF (8 mL) at −78 °C. The mixture was allowed to warm to room temperature and stirred for 1 hour before it was cooled to −78 °C. α, α-Dichloro-*o*-xylene (0.16 g, 0.89 mmol) in THF (5 mL) was added dropwise. The mixture was allowed to warm to RT and stirred for 16 hours. The volatiles were removed *in vacuo* to give a white solid. Pyrrolidine (5 mL) was added and the mixture heated to 50 °C for 16 hours. After this time the pyrrolidine was removed *in vacuo* and the mixture washed with MeOH (3 × 5 mL) filtered and dried to give a white solid. Yield = 0.43 g (91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 – 7.40 (2H, m, Ar*H*), 7.10 – 7.03 (2H, m, Ar*H*), 3.99 – 3.84 (8H, m, C*H*$_2$O), 3.10 (4H, s, C*H*$_2$), 1.74 – 1.65 (8H, m, C*H*$_2$), 1.27 (12H, d, $^{3}J_{HP}$ = 5.3 Hz, C*H*$_3$) and 1.21 ppm (12H, d, $^{3}J_{HP}$ = 17.4 Hz, C*H*$_3$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 137.9 (dd, $^{2}J_{CP}$ = 8.0 Hz, $^{3}J_{CP}$ = 3.0 Hz, ArC_q), 131.1 (d, $^{3}J_{CP}$ = 11.4 Hz, Ar*C*), 125.7 (d, $^{4}J_{CP}$ = 1.6 Hz, Ar*C*), 110.0 (s, O$_2$*C*$_q$), 64.5 (s, *C*H$_2$O), 63.6 (s, *C*H$_2$O), 47.6 (d, $^{2}J_{CP}$ = 6.9 Hz, *C*H$_2$), 32.3 (d, $^{2}J_{CP}$ = 25.7 Hz, C*H*$_3$), 31.2 (d, $^{2}J_{CP}$ = 17.4 Hz, C*H*$_3$), 25.8 (s, C_q) and 25.6 ppm (dd, $^{1}J_{CP}$ = 26.3 Hz, $^{4}J_{CP}$ = 7.3 Hz, PC*H*$_2$). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 6.0 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 585.3581; found 585.3580. Elem. Anal. Calcd for $C_{30}H_{48}O_4P_2$: C, 67.39; H, 9.05. Found: C, 65.20; H, 8.82.

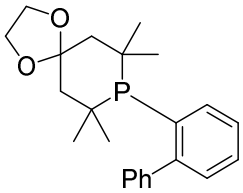
Example 37: Synthesis of bis(2,2,6,6,-tetramethylphoshorinone)xylene, BPX.



1,2-Bis((7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decan-8-yl)methyl)benzene (0.77 g, 1.44 mmol) was stirred in acetic acid (15 mL) at 120 °C for 3 hours. After this time the volatiles were removed *in vacuo* and the crude material recrystallized from MeOH to give a white solid. Yield = 0.37 g (58%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (2H, ddd, $^{3}J_{HH}$ = 5.9 Hz, $^{3}J_{HH}$ = 3.8 Hz, $^{4}J_{HP}$ = 2.4 Hz, Ar*H*), 7.16 – 7.11 (2H, m, Ar*H*), 3.24 (4H, s, C*H*$_2$P), 2.54 (4H, dd, $^{2}J_{HH}$ = 12.4 Hz, $^{3}J_{HP}$ = 4.4 Hz, C*H*$_2$), 2.35 (4H, dd, $^{2}J_{HH}$ = 12.5 Hz, $^{3}J_{HP}$ = 16.8 Hz, C*H*$_2$), 1.20 (12H, d, $^{3}J_{HP}$ = 5.4 Hz, C*H*$_3$) and 1.07 ppm (12H, d, $^{3}J_{HP}$ = 17.0 Hz, C*H*$_3$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 210.0 (d, $^{3}J_{CP}$ = 1.3 Hz, *C*=O), 136.9 (dd, $^{2}J_{CP}$ = 7.7 Hz, $^{3}J_{CP}$ = 2.8 Hz, ArC_q), 131.3 (d, $^{3}J_{CP}$ = 11.2 Hz, Ar*C*), 126.4 (d, $^{4}J_{CP}$ = 1.8 Hz, Ar*C*), 55.5 (d, $^{2}J_{CP}$ = 6.4 Hz, *C*H$_2$C=O), 35.3 (d,

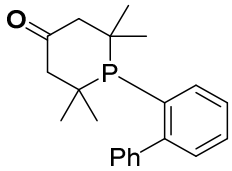
$^{1}J_{CP}$ = 19.2 Hz, *C*$(CH_3)_2$), 31.7 (d, $^{2}J_{CP}$ = 25.2 Hz, *C*H_3), 26.4 (dd, $^{1}J_{CP}$ = 26.6 Hz, $^{4}J_{CP}$ = 8.7 Hz, *C*H_2P) and 25.8 ppm (s, *C*H_3). $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 5.5 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 447.2581; found 447.2575.

Example 38: Synthesis of 8-([1,1'-biphenyl]-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane



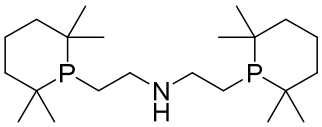
7,7,9,9-Tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane (0.34 g, 1.57 mmol), [1,1'-biphenyl]-2-yl trifluoromethanesulfonate (0.34 g, 1.12 mmol), palladium(II) acetate (1.26 mg, 0.006 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.34 g, 2.24 mmol) were dissolved in toluene (5 mL) and heated to 85 °C for 16 hours. After this time a ^{31}P NMR spectrum was recorded and it revealed approximately 60% conversion to the desired product. Additional palladium(II) acetate was added (1.26 mg, 0.006 mmol) and the mixture heated at 110 °C for a further 16 hours. After this time the clear dark orange solution was further diluted with toluene (3 mL) and washed with degassed water (3 × 5 mL). It was then dried over $MgSO_4$, filtered and evaporated to dryness. The crude material was washed with methanol (3 mL) to give a pale brown precipitate. Yield = 0.20 g (35%) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (1H, d, $^{3}J_{HP}$ = 7.6 Hz, Ar*H*), 7.39 – 7.20 (8H, m, Ar*H*), 4.03 – 3.90 (4H, m, C*H*$_2$O), 2.08 (2H, dd, $^{2}J_{HH}$ = 14.3 Hz, $^{2}J_{HP}$ = 2.3 Hz, C*H*), 1.65 (2H, dd, $^{2}J_{HH}$ = 14.4 Hz, $^{2}J_{HP}$ = 5.6 Hz, C*H*), 1.25 (6H, d, $^{3}J_{HP}$ = 19.3 Hz, C*H*$_3$) and 0.84 ppm (6H, d, $^{3}J_{HP}$ = 10.1 Hz, C*H*$_3$). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 151.9 (d, $^{2}J_{CP}$ = 34.3 Hz, Ar*C*$_q$Ph), 143.8 (d, $^{3}J_{CP}$ = 8.1 Hz, Ar*C*$_q$P), 135.6 (d, $^{1}J_{CP}$ = 31.1 Hz, Ar*C*$_q$), 134.1 (d, $^{3}J_{CP}$ = 4.1 Hz, Ar*C*H), 131.0 (d, $^{2}J_{CP}$ = 5.9 Hz, Ar*C*), 130.8 (d, $^{3}J_{CP}$ = 4.6 Hz, Ar*C*H), 128.6 (s, Ar*C*H), 127.4 (s, Ar*C*H), 126.6 (s, Ar*C*H), 111.2 (s, O_2C_q), 64.9 (s, *C*H_2O), 63.3 (s, C*H*$_2$O), 44.5 (d, $^{2}J_{CP}$ = 1.7 Hz, C_qCH_2), 32.0 (d, $^{2}J_{CP}$ = 36.3 Hz, *C*H_3), 31.5 (d, $^{1}J_{CP}$ = 19.3 Hz, *C*$(CH_3)_2$) and 31.2 ppm (d, $^{2}J_{CP}$ = 7.4 Hz, *C*H_3). $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ −8.4 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 369.1983; found 369.1974.

Example 39: Synthesis of 1-([1,1'-biphenyl]-2-yl)-2,2,6,6-tetramethylphosphinan-4-one



8-([1,1'-Biphenyl]-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane (50 mg, 0.15 mmol) was dissolved in acetic acid (2.0 mL) and heated to 120 °C for 16 hours. After this time the volatiles were removed *in vacuo* to give a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (1H, d, $^{3}J_{HH}$ = 7.2 Hz, Ar*H*), 7.43 – 7.22 (6H, m, Ar*H*), 7.22 – 7.09 (2H, m, Ar*H*), 2.86 (2H, dd, $^{2}J_{HH}$ = 12.9 Hz, $^{3}J_{HP}$ = 2.4 Hz, C*H*$_2$), 2.21 (2H, dd, $^{2}J_{HH}$ = 13.0 Hz, $^{3}J_{HP}$ = 4.8 Hz, C*H*$_2$), 1.09 (6H, d, $^{3}J_{HP}$ = 18.6 Hz, C*H*$_3$) and 0.88 ppm (6H, $^{3}J_{HP}$ = 10.0 Hz, C*H*$_3$). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 212.0 (s, *C*=O), 152.3 (d, $^{2}J_{CP}$ = 34.8 Hz, Ar*C*$_q$Ph), 143.3 (d, $^{3}J_{CP}$ = 8.0 Hz, Ar*C*$_q$), 134.5 (d, $^{1}J_{CP}$ = 30.3 Hz, Ar*C*$_q$), 133.5 (d, $^{3}J_{CP}$ = 4.0 Hz, Ar*C*H), 131.3 (d, $^{4}J_{CP}$ = 6.0 Hz, Ar*C*H), 130.8 (d, $^{4}J_{CP}$ = 4.4 Hz, Ar*C*H), 129.2 (s, Ar*C*H), 127.5 (s, Ar*C*H), 127.0 (s, Ar*C*H), 126.8 (s, Ar*C*H), 53.5 (s, *C*H$_2$), 35.9 (d, $^{1}J_{CP}$ = 21.8 Hz, *C*(CH$_3$)$_2$), 32.0 (d, $^{2}J_{CP}$ = 34.6 Hz, *C*H$_3$) and 30.0 ppm (d, $^{2}J_{CP}$ = 7.6 Hz, *C*H$_3$). ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ −3.5 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 325.1721; found 325.1715.

Example 40: Synthesis of bis(2-(2,2,6,6-tetramethylphosphinan-1-yl)ethyl)amine



TMP (2.80 g, 17.7 mmol) was dissolved in THF (40 mL). The mixture was cooled to –50°C and *n*-BuLi (2.0M in cyclohexane, 9.73 mL, 19.5 mmol) was added dropwise. The clear yellow solution was allowed to warm to RT and stirred for 5 hours. After this time the mixture was again cooled to –50°C and $(CH_3)_3SiN(CH_2CH_2Cl)_2$ (1.33 g, 6.2 mmol) in THF (5 mL) was added dropwise. After stirring for 15 minutes the mixture was allowed to warm to RT and then heated to 50°C for 24 hours. The volatiles were then removed *in vacuo* and then heptane (40 mL) and DI H_2O (40 mL) was added. The vigorously stirred biphasic mixture was heated at 60°C for 72 hours. After this time the heptane layer was separated and then the aqueous portion was extracted with Et_2O (2 × 30 mL). The combined organics were then dried ($MgSO_4$) and evaporated to yield an oil. The oil was subjected to vacuum distillation to give the product as a pale yellow viscous oil. Yield = 1.25 g (52%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.91 – 2.65 (4H, m, NC*H*$_2$), 1.61 (4H, td, $^{3}J_{HH}$ = 8.2 Hz, $^{2}J_{HP}$ = 3.9

Hz, PCH_2), 1.56 – 1.35 (12H, m, CH_2CH_2CH_2), 1.10 (12H, d, $^3J_{HP}$ = 17.2 Hz, CH_3) and 1.04 ppm (12H, d, $^3J_{HP}$ = 7.2 Hz, CH_3). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 49.7 (d, $^2J_{CP}$ = 28.5 Hz, NCH_2), 39.8 (br. s, CH_2C_q), 31.1 (d, $^1J_{CP}$ = 26.9 Hz, C$(CH_3)_2$), 29.0 (d, $^2J_{CP}$ = 13.8 Hz, CH_3), 26.5 (br. s. CH_3), 21.5 (d, $^1J_{CP}$ = 21.8 Hz, PCH_2) and 20.4 ppm (d, $^3J_{Cp}$ = 1.1 Hz, CH_2CH_2CH_2). $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 3.7 ppm. HR-MS (+ve ESI): m/z (calc.) $[M+H]^+$ 386.3106; found 386.3094.

It will be appreciated that many further modifications and permutations of various aspects of the described embodiments are possible. Accordingly, the described aspects are intended to embrace all such alterations, modifications, and variations that fall within the spirit and scope of the appended claims.

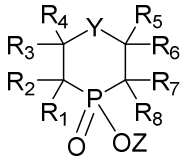
Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

Throughout this specification and the claims which follow, unless the context requires otherwise, the phrase "consisting essentially of", and variations such as "consists essentially of" will be understood to indicate that the recited element(s) is/are essential i.e. necessary elements of the invention. The phrase allows for the presence of other non-recited elements which do not materially affect the characteristics of the invention but excludes additional unspecified elements which would affect the basic and novel characteristics of the method defined.

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

Claims

1. A method of synthesising a phosphorus compound of Formula (I), a salt, solvate or stereoisomer thereof:



(I)

wherein Y is selected from an optionally substituted C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene, optionally substituted silylene, optionally substituted aminoylene, acylene, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^{+}(R_9R_{10})-$;

Z is selected from H, optionally substituted alkyl or a metal cation;

R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

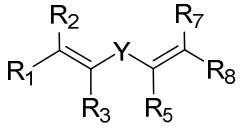
wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;

R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl;

the method comprising:

a) reacting a compound of Formula (A) with a hypophosphite ester, acid, salt or solvate thereof and an organosilicon compound, the compound of Formula (A) is



(A)

wherein Y is selected from an optionally substituted C_{1-10} alkylene, optionally substituted

C_{1-10} alkenylene, optionally substituted silylene, optionally substituted amino, acylene, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or -$P^+(R_9R_{10})$-;

wherein R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

wherein R_1 and R_8 can be linked to form an optionally substituted cyclo moiety;

R_3 and R_5 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl.

2. The method according to claim 1, wherein the hypophosphite ester, acid, salt or solvate thereof is selected from hypophosphorous acid (H_3PO_2), ammonium hypophosphite ($NH_4H_2PO_2$) and sodium hypophosphite ($NaPO_2H_2$), potassium hypophosphite, calcium bis(hypophosphite), copper hypophosphite, nickel(II) bis(hypophosphite), magnesium hypophosphite, anilinium hypophosphite, methyl hypophosphite, ethyl hypophosphite, or a combination thereof.

3. The method according to claim 1 or 2, wherein the organosilicon compound is selected from bis(trimethylsilyl)amine (HMDS), *N,N*-Bis(trimethylsilyl)methylamine, bis(dimethylamino)dimethylsilane, N,O-bis(trimethylsilyl)acetamide (BSA), N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA), *N,N*-dimethyltrimethylsilylamine, hexamethyldisiloxane, *N,N*-diethyltrimethylsilylamine 1-(trimethylsilyl)pyrrolidine trimethylsilyl chloride (TMSCl), trimethylsilyl bromide (TMSBr), chlorotriethylsilane, and a combination thereof.

4. The method according to any one of claims 1 to 3, wherein a molar ratio of hypophosphite ester, acid, salt or solvate thereof to the organosilicon compound is 1:10 to 1:1.

5. The method according to any one of claims 1 to 4, wherein the step of reacting a compound of Formula (A) with the hypophosphite ester, acid, salt or solvate thereof and the organosilicon compound further comprises a base.

6. The method according to claim 5, wherein the base is selected from triethylamine, diethylamine, Hünigs base, pyrrolidine, pyridine, lutidine, piperidine 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,4-diazabicyclo[2.2.2]octane (DABCO), sodium hydroxide, potassium hydroxide, ammonium hydroxide, sodium carbonate, sodium hydrogen carbonate, barium hydroxide, calcium carbonate, caesium carbonate, or a combination thereof.

7. The method according to any one of claims 1 to 6, wherein the step of reacting a compound of Formula (A) with the hypophosphite ester, acid, salt or solvate thereof and the organosilicon compound further comprises a solvent.

8. The method according to claim 7, wherein the solvent is selected from tetrahydrofuran (THF), toluene, xylenes, methylene chloride, dichloroethane, tetrachloroethane, ethers, dimethylacetamide (DMA), or a combination thereof.

9. The method according to any one of claims 1 to 8, the method further comprises a step of treating a product of step (a) with an acid.

10. The method according to any one of claims 1 to 9, wherein the compound of Formula (A) is reacted with the hypophosphite ester, acid, salt or solvate thereof and the organosilicon compound at a temperature of 70 °C to 150 °C.

11. The method according to any one of claims 1 to 10, the method further comprises a step (b) after (a) of modifying the compound of formula (I) at the Y moiety.

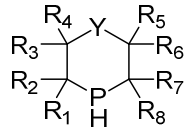
12. The method according to any one of claims 1 to 11, the method further comprises a step (b) after (a) of modifying the compound of formula (I) with a protecting group compound.

13. The method according to claim 12, wherein the protecting group compound is selected from ethylene glycol, methanol, ethanol, propylene glycol, 2,2-dimethyl-1,3-

propanediol (neopentylglycol), dimethyl hydrazine, 1,2-ethanedithiol and 1,3-propanedithiol.

14. The method according to any one of claims 1 to 13, the method further comprises a step of reducing the compound of formula (I).

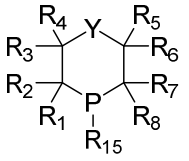
15. The method according to any one of claims 1 to 14, the method further comprises a step reducing the phosphorus compound of Formula (I) in order to form a phosphorus compound of Formula (II):



(II)

wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and Y are as disclosed herein.

16. The method according to any one of claims 1 to 15, the method further comprises of functionalising the compound of Formula (II) in order to form a phosphorus compound of Formula (III):

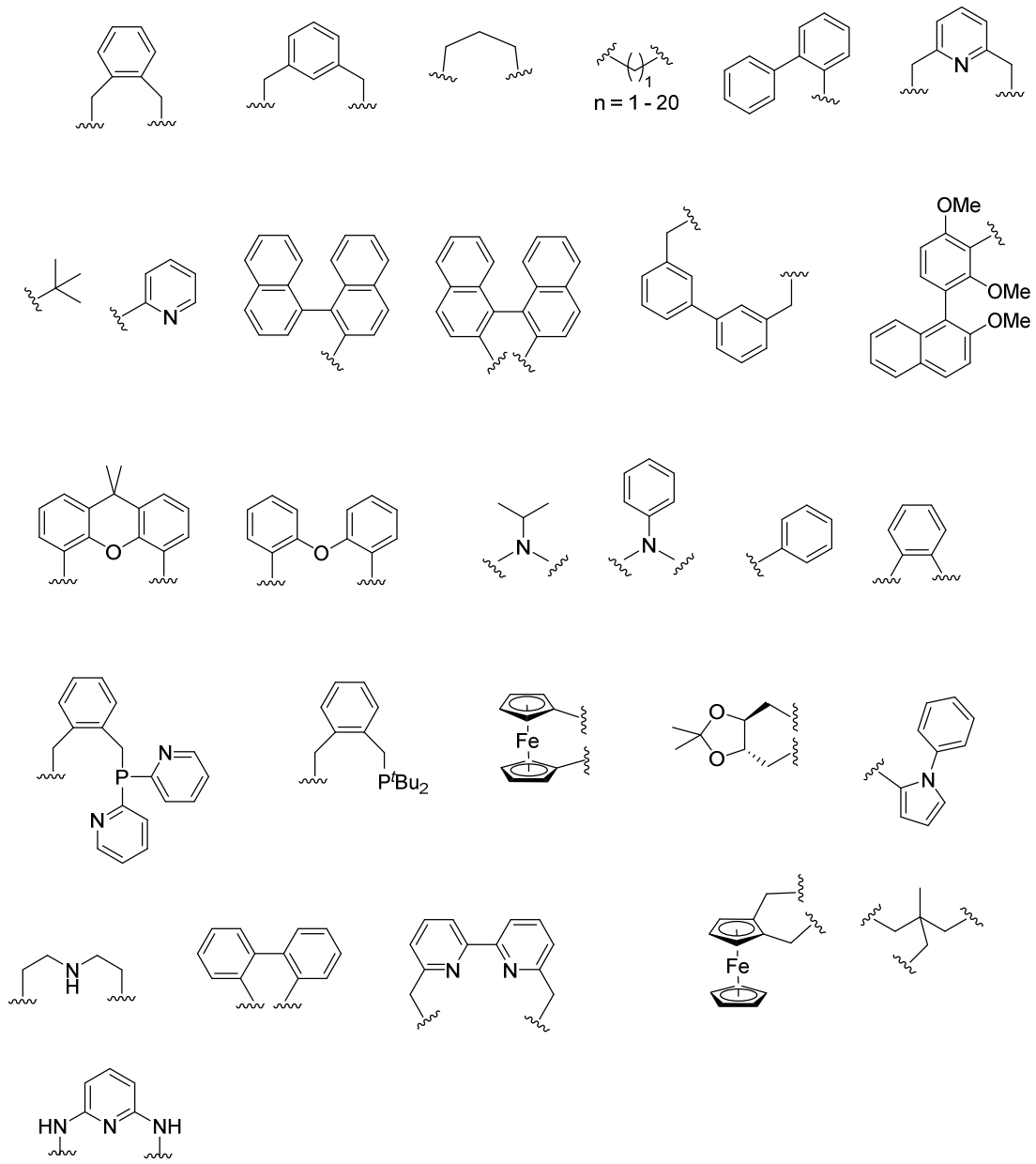


(III)

wherein R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and Y are as disclosed herein;
R_{15} is selected from halo, oxo, optionally substituted amino, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl.

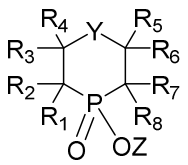
17. The method according to claim 16, wherein the optional substituent at R_{15} comprises another compound of Formula (III).

18. The method according to claim 16 or 17, wherein the optional substituent at R_{15} is selected from:



wherein ~ represents a bond to R_{15} of compound of Formula (III).

19. A phosphorus compound of Formula (I), a salt, solvate or stereoisomer thereof:



(I)

wherein Y is selected from an optionally substituted C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene, optionally substituted silylene, optionally substituted amino, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^{+}(R_9R_{10})-$;

Z is selected from H, optionally substituted alkyl or a metal cation;

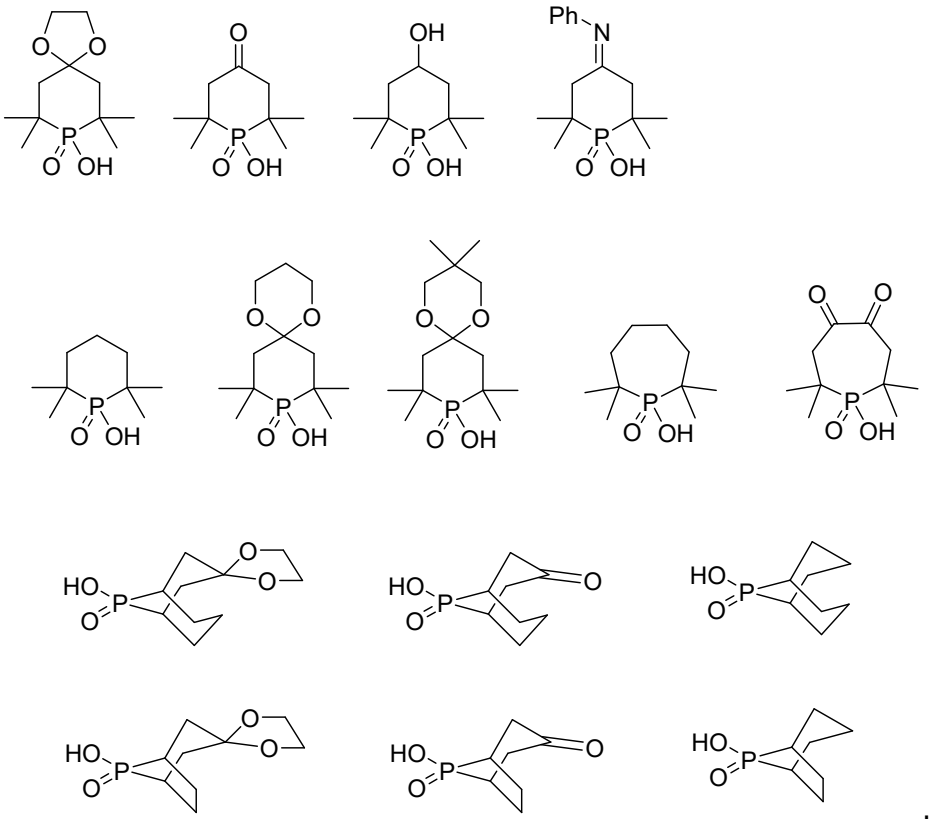
R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;

R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl; and

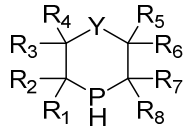
R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl.

20. The compound of Formula (I) according to claim 19, selected from:



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21. A phosphorus compound of Formula (II), a salt, solvate or stereoisomer thereof:



(II)

wherein Y is selected from an C_{1-10} alkylene, optionally substituted C_{1-10} alkenylene, optionally substituted silylene, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or -$P^{+}(R_9R_{10})$-;

R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

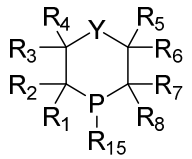
wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;

R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino,

optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl.

22. A phosphorus compound of Formula (III), a salt, solvate or stereoisomer thereof:



(III)

wherein Y is selected from an C_{1-10} alkylene optionally substituted with acyl or 1,2-ethanedioxy or 1,3-propanedioxy or 2,2-dimethyl-1,3-propanedioxy, optionally substituted C_{1-10} alkenylene, optionally substituted silylene, thioacylene, sulfinylene, sulfonylene, -P(O)(OZ)- or $-P^+(R_9R_{10})-$;

R_1, R_2, R_7 and R_8 are independently selected from oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

wherein R_1 and R_8 can be linked to form an optionally substituted cycloalkyl;

R_3, R_4, R_5, and R_6 are independently selected from H, oxo, halo, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted haloalkyl; optionally substituted alkynyl; optionally substituted oxyalkyl; optionally substituted amino, optionally substituted thio, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, and optionally substituted aryl;

R_9 and R_{10} are independently selected from H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloyl, optionally substituted aryl, optionally substituted heteroaryl; and

R_{15} is selected from halo, oxo, optionally substituted amino, alkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, optionally substituted m-

xylenyl, optionally substituted pyridinylmethyl, optionally substituted biphenylmethyl, 2-(compound of Formula (III))biphenyl, optionally substituted binaphthyl, optionally substituted phenylnaphthyl, optionally substituted diphenyl oxide, and another compound of Formula (III).

23. The compound of Formula (I), (II) or (III) according to any one of claims 19 to 22, selected from:

