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(54) Title: A process for preparing tertiary phosphines

(57) Abstract: The present invention relates to a process for the conversion of a tertiary phosphine oxide to the corresponding tertiary phosphine. The process has desired characteristics such as inexpensiveness, ease of handling, high efficiency, high yield and high conversion, as well as low environmental impact.



WO 2020/077582 A1

A process for preparing tertiary phosphines

TECHNICAL FIELD

The present invention relates to a process for the conversion of a tertiary phosphine oxide to the corresponding tertiary phosphine.

BACKGROUND

5 Phosphines, the phosphorous analogues of organic amines, constitute a class of highly important compounds with widespread industrial applicability within numerous areas. For example, tricycloalkylphosphine such as tricyclohexylphosphine is commonly used as a ligand in organometallic chemistry.

10 Preparation of tertiary phosphines from corresponding tertiary phosphine oxides by reduction reaction has been known for many years. Silanes like Ph_2SiH_2 , SiHCl_3 and $(\text{EtO})_3\text{SiH}$ have been used as reducing reagent in this reduction reaction and give the expected phosphines with ideal yields, such as the reaction reported by *Chem. Ber.* 1965, 171-174. Unfortunately, several
15 silanes have been demonstrated harmful since they generate a dangerous, pyrophoric and toxic SiH_4 gas.

 It is reported by *J. Am. Chem. Soc.* 2012, 134, 18325-18329, *Tetrahedron* 2012, 68, 3151-3155, *Organometallics* 2016, 35, 1030-1035 and *ChemCatChem* 2017, 9, 4460-4464 that Lewis or Brønsted acids can be employed as catalysts or
20 additives in the reduction reaction with silanes. The use of Lewis or Brønsted acids can help improve the process, such as shortening reaction time or decreasing reaction temperature. However, strict anhydrous reaction condition is desired since those acids are quite hydroscopic.

 U.S. Patent Application No. 2010137643A1 discloses a process for
25 preparing cyclohexyl-substituted phosphines. According to the example, tricyclohexylphosphine oxide was converted to tricyclohexylphosphine hydrochloride with the help of phosgene and H_2 . Tricyclohexylphosphine is then obtained by deprotonation of tricyclohexylphosphine hydrochloride with NaOH. Disadvantageously, phosgene is a highly toxic gas, which leads to difficulty in
30 handling and low susceptibility for industrial application.

 PCT Publication WO 2017041723 and *Angew. Chem. Int. Ed.* 2017, 56, 15989-15992 disclose a method for converting phosphine oxides to

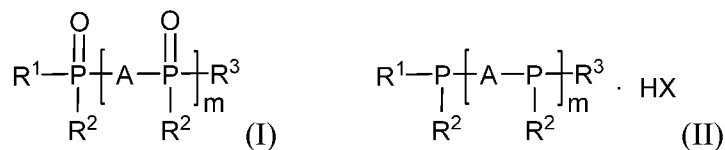
corresponding phosphines under mild reduction reaction. However, the yield of trialkylphosphine obtained by this method is relatively low.

There is still a need to provide a process to prepare alkyl or alkenyl substituted phosphines with desired characteristics such as inexpensiveness, ease of handling, high efficiency, high yield and high conversion, as well as low environmental impact, which can overcome the drawbacks in prior arts.

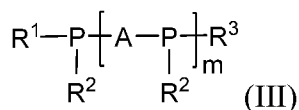
SUMMARY OF THE INVENTION

The present invention therefore pertains to a process for the conversion of a tertiary phosphine oxide to the corresponding tertiary phosphine, comprising following steps:

- (i) reacting a tertiary phosphine oxide having general formula (I) with phosphorous acid or a phosphite compound, in the presence of a halogen compound and a solvent to obtain a reaction mixture comprising a slurry comprising a tertiary phosphine hydrogen halide salt having general formula (II);



- (ii) isolating the slurry obtained at step(i) from the reaction mixture;
- (iii) reacting the slurry obtained at step(ii) with a base to obtain the corresponding tertiary phosphine having general formula (III);



wherein:

- R^1 , R^2 and R^3 are each independently a branched, linear or cyclic $\text{C}_1\text{-C}_{20}$ alkyl or alkenyl, which is optionally interrupted by one or several heteroatoms;
- A is a linking moiety;
- m is an integer of 0 to 2;
- X is a halogen atom.

DEFINITIONS

Throughout the description, including the claims, the term "comprising one" should be understood as being synonymous with the term "comprising at least one", unless otherwise specified, and "between" should be understood as
5 being inclusive of the limits.

As used herein, the terminology "(C_n-C_m)" in reference to an organic group, wherein n and m are each integers, indicates that the group may contain from n carbon atoms to m carbon atoms per group.

The articles "a", "an" and "the" are used to refer to one or to more than one
10 (i.e., to at least one) of the grammatical object of the article.

The term "and/or" includes the meanings "and", "or" and also all the other possible combinations of the elements connected to this term.

It is specified that, in the continuation of the description, unless otherwise indicated, the values at the limits are included in the ranges of values which are
15 given.

Ratios, concentrations, amounts, and other numerical data may be presented herein in a range format. It is to be understood that such range format is used merely for convenience and brevity and should be interpreted flexibly to include
20 not only the numerical values explicitly recited as the limits of the range, but also to include all the individual numerical values or sub-ranges encompassed within that range as if each numerical value and sub-range is explicitly recited.

The terms "halogen" or "halo", as used herein usually refer to F, Cl, Br and I.

The terms "phosphite compound" as used herein, refer to a compound
25 derived from phosphorous acid H₃PO₃, such as a phosphite ester, an organophosphorus compound with the formula P(OR)₃.

DETAILS OF THE INVENTION

Step(i)

It is contemplated that any tertiary phosphine oxide having general formula
30 (I) may be reduced by the inventive process, notably by a proper selection of phosphorous acid or the phosphite compound.

The heteroatom interrupting alkyl or alkenyl represented by R¹, R² and R³ is preferably N, O, Si or S.

Preferably, R¹, R² and R³ are each independently an alkyl or an alkenyl
35 group as such, meaning that it is not interrupted by one or several heteroatoms.

As used herein, the term "alkyl" means a saturated hydrocarbon radical, which may be linear, branched or cyclic.

Advantageously, R^1 , R^2 and R^3 are each independently chosen in the group consisting of methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl and decyl.

Preferably, R^1 , R^2 and R^3 are each independently a 3-10 membered cycloalkyl and more preferably a 5-6 membered cycloalkyl, which is not interrupted by one or several heteroatoms.

Advantageously, R^1 , R^2 and R^3 are each independently chosen in the group consisting of cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl.

As used herein, the term "alkenyl" as a group or part of a group denotes an aliphatic hydrocarbon group containing at least one carbon-carbon double bond and which may be linear, branched or cyclic.

Preferably, R^1 , R^2 and R^3 are each independently an alkenyl group which comprising less than two carbon-carbon double bonds. Exemplary alkenyl groups include, but are not limited to, ethenyl, propenyl, butenyl, pentenyl, hexenyl, heptenyl, octenyl, nonenyl, cyclobutenyl, cyclopentenyl, cyclohexenyl, cycloheptenyl and cyclooctenyl.

It can be understood by a skilled person that the cycloalkyl or the cycloalkenyl may be a polycyclic ring system, having two or more rings, *e.g.* bicyclic, tricyclic or tetracyclic, including bridged or fused cycles, as well as spiro cycles.

The linking moiety A may be any diradical capable of attaching the two phosphorous atoms of the phosphine (oxide) functions to each other, through any number of intervening bonds. The linking moiety A may comprise substituted or unsubstituted hydrocarbylene or substituted or unsubstituted monocyclic or polycyclic carbocyclylene or heterocyclylene, and optionally one or several functional groups, such as ether or thioether function.

When m in formula (I) is more than 1, A is independently selected at each occurrence.

In one embodiment, A is a polycyclic diradical, such as a diradical comprising 2 to 8 ring moieties, *e.g.* 2 to 6, or 2 to 4 ring moieties, wherein each ring moiety is independently selected from 5- or 6-membered, saturated or unsaturated, aromatic or non-aromatic carbocycles and heterocycles, and wherein the ring moieties are either fused to each other or attached to each other through one or several intervening bonds of covalent type or metallocene type, such as a

covalent bond, an ether function, a thioether function, an optionally substituted alkylene group, *e.g.* a methylene or ethylene group, or a ferrocene type bond. In this embodiment, the two phosphine oxide functions preferably are attached to different ring moieties.

5 In another embodiment, A may be a substituted or unsubstituted hydrocarbylene, carbocyclylene, or heterocyclylene. The linking moiety A also may be a substituted or unsubstituted metallocenylene, *i.e.* a diradical derived from a metallocene, *i.e.* a compound with the general formula $(C_5H_5)_2M$ consisting of two cyclopentadienyl anions bound to a positively charged metal
10 centre (M). As an example, A may be a substituted or unsubstituted ferrocenylene.

In one embodiment, A is an unsubstituted or substituted diradical selected from the group of substituted or unsubstituted, saturated or unsaturated, branched or linear C_1 - C_{20} alkylene, C_3 - C_{20} carbocyclylene, *e.g.* C_6 - C_{20} arylene, 5-20
15 membered heterocyclylene, *e.g.* 5-20 membered heteroarylene, C_6 - C_{40} bicycylene, *e.g.* C_{12} - C_{40} biarylene, 10-40 membered biheterocyclylene, *e.g.* 10-40 membered biheteroarylene, and C_{10} - C_{30} ferrocenylene.

For example, A may be an unsubstituted or a substituted diradical selected from the group of C_6 - C_{20} arylene, 5-20 membered heterocyclylene, 5-20
20 membered heteroarylene, C_{12} - C_{40} biarylene, 10-40 membered biheterocyclylene, 10-40 membered biheteroarylene, and C_{10} - C_{30} ferrocenylene.

In one embodiment, A is an unsubstituted or a substituted diradical selected from the group of C_{12} - C_{40} biarylene, 5-20 membered heterocyclylene and C_{10} - C_{30} ferrocenylene, *e.g.* binaphthyl, such as 2,2'-binaphthyl; xanthenylene,
25 *e.g.* 4,5-xanthenylene; and (C_{10}) ferrocenylene, *e.g.* 1,1'-ferrocenylene.

In one embodiment, m in formula (I) is 0, and the tertiary phosphine oxide according to the present invention may then be represented by the general formula (I') as follow:



R^1 , R^2 and R^3 are as defined herein above.

Examples of the tertiary phosphine oxide having general formula (I') are trimethylphosphine oxide, dimethylethylphosphine oxide, triethylphosphine

oxide, tripropylphosphine oxide, tributylphosphine oxide, tri-*tert*-butylphosphine oxide, tripentylphosphine oxide, trihexylphosphine oxide, triheptylphosphine oxide, trioctylphosphine oxide, tricyclopropylphosphine oxide, tricyclobutylphosphine oxide, tricyclopentylphosphine oxide,
 5 tricyclohexylphosphine oxide, tricycloheptylphosphine oxide, tricyclooctylphosphine oxide, dicyclohexylmethylphosphine oxide.

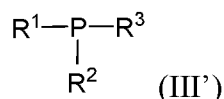
In another embodiment, *m* in formula (I) is 1, and the tertiary phosphine oxide according to the present invention may then be represented by the formula (I''):



R^1 , R^2 and R^3 and A are as defined herein above.

Example of the tertiary phosphine oxide having general formula (I'') is ethane-1,2-diylbis(dicyclohexylphosphine oxide).

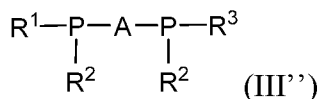
In one embodiment, *m* in formula (III) is 0, and the tertiary phosphine
 15 according to the present invention may then be represented by the general formula (III') as follow:



R^1 , R^2 and R^3 are as defined herein above.

20 Examples of the tertiary phosphine having general formula (III') are trimethylphosphine, dimethylethylphosphine, triethylphosphine, tripropylphosphine, tributylphosphine, tri-*tert*-butylphosphine, tripentylphosphine, trihexylphosphine, triheptylphosphine, trioctylphosphine, tricyclopropylphosphine, tricyclobutylphosphine, tricyclopentylphosphine,
 25 tricyclohexylphosphine, tricycloheptylphosphine, tricyclooctylphosphine, dicyclohexylmethylphosphine.

In one embodiment, *m* in formula (III) is 1, and the tertiary phosphine according to the present invention may then be represented by the general formula (III'') as follow:



R^1 , R^2 and R^3 and A are as defined herein above.

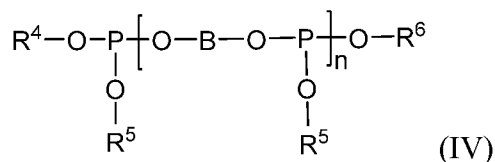
Example of the tertiary phosphine having general formula (III'') is 1,2-bis(dicyclohexylphosphino)ethane.

5 The reducing phosphite compound may comprise at least one phosphite function, such as a secondary phosphite function and/or a tertiary phosphite function. The phosphite compound of the invention may comprise at least one or several secondary phosphite functions and/or one or several tertiary phosphite functions. The phosphorus atom of each phosphite function may be linked to
10 groups selected from substituted or unsubstituted, branched or linear hydrocarbyl; and substituted or unsubstituted carbocyclyl or heterocyclyl, as defined herein above.

For example, the phosphite compound may contain from 1 to 3 phosphite functions. In one embodiment, the phosphite compound contains 1 or 2
15 phosphite functions. In one particular embodiment, the phosphite compound is a tertiary phosphite that contains 1 phosphite function.

Furthermore, it is contemplated that the phosphite compound may additionally contain other functional groups, such as halogen, nitro, amino, cyano, ether, thioether or alkylene group.

20 In one embodiment, the phosphite compound is represented by the general formula (IV) as follow:



wherein R^4 , R^5 and R^6 are each independently selected from the group comprising: hydrogen, substituted or unsubstituted, branched or linear
25 hydrocarbyl; and substituted or unsubstituted, aliphatic or aromatic carbocyclyl or heterocyclyl; B is a linking moiety; and n is an integer of from 0 to 2, such as 0 or 1.

Preferably, at least one of the R^4 , R^5 and R^6 group is not a hydrogen atom.

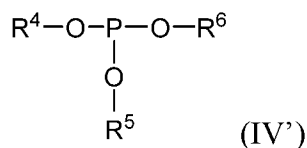
For example, R^4 , R^5 and R^6 may be independently selected from the group
30 comprising: hydrogen atom, substituted or unsubstituted, branched or linear C_1 - C_{20} hydrocarbyl, e.g. C_1 - C_{10} hydrocarbyl, e.g. C_1 - C_6 hydrocarbyl; and substituted

or unsubstituted, aliphatic or aromatic C₃-C₂₀ carbocyclyl, *e.g.* C₃-C₁₀ carbocyclyl, or C₃-C₆ carbocyclyl, or 5-20 membered heterocyclyl, *e.g.* 5-10 membered heterocyclyl, or 5-6 membered heterocyclyl.

In one embodiment, R⁴, R⁵ and R⁶ are independently selected from the group comprising: hydrogen atom, substituted or unsubstituted, branched or linear C₁-C₂₀ hydrocarbyl, *e.g.* C₁-C₁₀ hydrocarbyl, *e.g.* C₁-C₆ hydrocarbyl; and substituted or unsubstituted, aliphatic C₃-C₂₀ carbocyclyl, *e.g.* C₃-C₁₀ carbocyclyl, or C₃-C₆ carbocyclyl. For example, any hydrocarbyl moiety may be an alkyl and any carbocyclyl moiety may be a cycloalkyl.

More particularly, R⁴, R⁵ and R⁶ may be each independently selected from the group comprising: hydrogen atom, substituted or unsubstituted C₆-C₂₀ aryl-C₀-C₂₀ alkyl, *e.g.* substituted or unsubstituted C₆-C₂₀ aryl, such as substituted or unsubstituted phenyl or naphthyl, in particular substituted or unsubstituted phenyl.

In one embodiment, n in formula (IV) is 0, in which case the phosphite compound may be represented by the general formula (IV') as follow:



R⁴, R⁵ and R⁶ are as defined herein above.

Preferably, the phosphite compounds are chosen in the group consisting of: triphenylphosphite, diphenylphosphite, phenylphosphite, diisodecylphenylphosphite, diphenylisodecylphosphite, diisooctyloctylphenylphosphite, phenyldiisodecylphosphite, tris(4-methoxyphenyl)phosphite, tri(*o*-tolyl)phosphite, tris(nonylphenyl)phosphite, tetraphenyldipropyleneglycoldiphosphate, 4,4'-isopropylidenediphenol C₁₂₋₁₅ alcohol phosphite and any combination thereof.

The phosphite compound is preferably present in an amount from 1 to 10 molar equivalent phosphite of the phosphite compound to the phosphine oxide of the tertiary phosphine oxide having general formula (I), preferably from 2 to 6 molar equivalent phosphite.

For example, the phosphite compound may suitably be present in an amount such as the molar ratio of the phosphite function(s) of the phosphite compound to the phosphine oxide function(s) of the tertiary phosphine oxide

having general formula (I) to be reduced is from 1 to 10, preferably from 1.5 to 8 and more preferably from 2 to 6.

The phosphorous acid is preferably present in an amount from 1 to 10 molar equivalent phosphorous acid to the phosphine oxide of the tertiary phosphine oxide having general formula (I), preferably from 2 to 6 molar equivalent.

In one embodiment, the phosphorous acid or the phosphite compound is attached to a solid support. In this embodiment, the phosphorous acid or the phosphite compound may be regenerated after use, *e.g.* by reacting it with a reduction agent, such as H_2 , $LiAlH_4$ and the like.

In accordance with the invention, the halogen compound can be any type of chemical species capable of forming a tertiary phosphine hydrogen halide salt. Said tertiary phosphine hydrogen halide salt is preferably a water soluble salt.

Preferably, the halogen compound comprises at least one halogen atom such as Cl, Br, I and F.

The halogen compound may be selected from the group comprising fluorine (F_2), chlorine (Cl_2), bromine (Br_2), iodine (I_2), iodine monochloride (ICl), iodine monobromide (IBr), heterocyclyl halides, such as N-halosuccinimide, 1,3-dihalo-5,5-dimethylhydantoin, haloalkanes, in particular tetrahalomethanes, such as tetrachloromethane, tetrabromomethane, tetraiodomethane, tetrafluoromethane, phosphine dihalides, tertiary phosphine dihalides, such as triphenylphosphine dichloride, triphenylphosphine dibromide, triphenylphosphine diiodide, triphenylphosphine difluoride, triphenylphosphine dichloride, and/or any trialkyl, cycloalkyl or aryl analogues thereof.

The halogen compound is preferably present in an amount from 0.1 to 1.2 molar equivalent of the tertiary phosphine oxide having general formula (I), in particular 0.2 to 1.0 molar equivalent, more preferably 0.3 to 1.0 molar equivalent.

The halogen compound may be present in any physical form, but suitable forms known to a person skilled in the art for a particular combination of reagents and/or reaction conditions that are naturally preferable.

The tertiary phosphine oxide having general formula (I), the phosphorous acid or the phosphite compound may be attached to a solid support. An example of such a solid support is a polystyrene material, such as sold under the trade name JandaJel™, by Sigma-Aldrich Co. Other possible solid phase supports are *e.g.* silica gel, Ring-Opening Olefin Metathesis Polymerization (ROMP) gel *etc.*

The person of ordinary skill in the art will know of various other possible solid supports, such as those described in US patent No. 7,491,779 by Steinke *et al.*, the contents of which are incorporated by reference.

5 The reaction in this step is carried out in the presence of solvent. It is understood by a skilled person that the solvent has good solubility towards the reactants and the halogen compound. Preferably, it is an anhydrous aprotic polar solvent.

10 Anhydrous aprotic solvent(s) may be chosen in the group consisting of toluene, hexane, tetrahydrofuran (THF), 2-methyltetrahydrofuran, acetonitrile, diethylether, dioxane, propionitrile, benzonitrile, ethyl acetate and mixtures of these.

The reaction medium may also comprise water, notably with a molar ratio of water to the tertiary phosphine oxide having general formula (I) ranging from 1/1 to 10/1, preferably from 1/1 to 2/1.

15 The reaction can also be carried out in the presence of a base. Said base is not particularly limited and can be an organic or inorganic base. Organic base may notably be tertiary amine chosen from a group consisting of pyridine, trimethylamine, triethylamine, DIPEA (N,N-diisopropylethylamine), DBU (1,8-diazabicyclo[5.4.0]undec-7-ene), DABCO (1,4-diazabicyclo[2.2.2]-octane) and
20 DMP (2,5-dimethylpyridine). Inorganic base may be alkali metal hydroxide, such as sodium hydroxide, potassium hydroxide and alkali metal salt chosen from a group consisting of sodium carbonate, sodium bicarbonate, potassium carbonate and potassium bicarbonate.

The bases mentioned above can be used solely or in the form of a mixture.

25 The base may be preferably present in an amount from 0.1 to 2 molar equivalents of the tertiary phosphine oxide having general formula (I) to be reduced, in particular 0.2 to 1.0 molar equivalents, more preferably 0.3 to 0.8 molar equivalents.

30 Further, the reaction can be carried out in virtually any type of reaction vessel, additionally increasing the versatility, specifically from an industrial perspective, of the invention.

The reaction of step(i) very advantageously may be carried out at a reaction temperature in the range of 25 to 45°C.

The reaction of step(i) may preferably be carried out under air or under an inert atmosphere, such as a nitrogen atmosphere. Very advantageously, the
5 reaction time may be from 2 to 11 hours and preferably from 2 to 7 hours.

Obviously, the process is more environmental-friendly since no toxic SiH_4 gas is generated and is more easily to be handled as all the reagents are quite stable in the presence of air or H_2O .

Step(ii)

10 The method for isolating the slurry obtained at step(i) from the reaction mixture is not particularly limited. For example, a skilled person can use several known techniques to realize the isolation, such as filtration or centrifugation, or even evaporating the solvent directly in order to obtain the slurry.

Preferably, the slurry may be washed by a solvent to remove the unreacted
15 reactant, by-products and so on. Said solvent can preferably be aprotic solvent chosen in the group consisting of toluene, pentane, hexane, cyclohexane, heptane, tetrahydrofuran (THF), 2-methyltetrahydrofuran, acetonitrile, diethyl ether, methyl tert-butyl ether (hereinafter MTBE), dioxane, propionitrile, benzonitrile, ethyl acetate and mixtures thereof.

Step(iii)

20 The base compound used in step(iii) can be an organic or inorganic base. It may notably be an inorganic base, which is chosen in the group consisting of sodium hydroxide, potassium hydroxide and mixtures thereof. It is also possible to use a salt, which is chosen in the group consisting of sodium carbonate,
25 sodium bicarbonate, potassium carbonate, potassium bicarbonate and mixtures thereof.

In a preferred embodiment, the base aqueous solution is prepared and then added to the slurry obtained at step(ii).

The reaction of step(iii) may preferably be carried out under air or under an inert atmosphere, such as a nitrogen atmosphere and argon atmosphere and preferably nitrogen atmosphere.

5 The reaction of step(iii) may preferably be carried out at a reaction temperature in the range of 20 to 25 °C.

Very advantageously, the reaction time of step(iii) may be from 0.2 and 1 hours.

10 Optionally, a solvent is added to extract the tertiary phosphine obtained at step(iii). Said solvent is aprotic solvent, consisting of toluene, pentane, hexane, cyclohexane, heptane, tetrahydrofuran (THF), 2-methyltetrahydrofuran, acetonitrile, diethyl ether, MTBE, dioxane, propionitrile, benzonitrile, ethyl acetate and mixtures thereof.

Preferably, the solvent is MTBE, toluene or hexane.

15 The following examples are included to illustrate embodiments of the invention. Needless to say, the invention is not limited to described examples.

EXPERIMENTAL PART

Materials

- Diphenyl phosphite (hereinafter DPPhite): CAS No.: 4712-55-4, 95% purity, J& K
- 20 - Triphenyl phosphite (hereinafter TPPhite): CAS No.: 101-02-0, 91% purity, J& K
- Tricyclohexylphosphine oxide (hereinafter $Cy_3P=O$): CAS No.: 13689-19-5, 98% purity, aladdin.
- I_2 : CAS No.: 7553-56-2, 99% purity, J& K
- 25 - Et_3N : CAS No.: 121-44-8, 99% purity, J& K
- THF: CAS No.: 109-99-9, anhydrous, J& K
- MTBE: CAS No.: 1634-04-4, anhydrous, J& K
- NaOH: CAS No.: 1310-73-2, Sinoreagent
- cyclohexane: CAS No.: 110-82-7, Sinoreagent

30 Example 1

Under N_2 atmosphere, 8.12 g DPPhite and 2.81 g TPPhite were loaded sequentially into a 150 mL Schlenk.

5.14 g $Cy_3P=O$ in 44.5 g anhydrous THF and 4.35 g I_2 were then added into the above Schlenk under N_2 atmosphere, respectively.

35 The reaction was stirred at 45 °C under N_2 atmosphere for 7 hours. THF was then removed from the reaction mixture in vacuo. The residual slurry was

thoroughly washed by MTBE for three times (15 g MTBE for 1st washing, and 10 g MTBE for 2nd and 3rd washing, respectively). As a result, the solution was removed by cannulation under N₂ and the rest solid was dried in vacuo for more than 1 hour.

5 Thus, 5.41 g pale white solid, namely pure tricyclohexylphosphine hydrogen iodide (hereinafter [Cy₃P·HI]) was obtained with an isolated yield of 78%.

In glovebox, a 5.30 g well-degassed 10 wt% NaOH aq. solution was added slowly into the above obtained [Cy₃P·HI] in 15 g well-degassed H₂O under stirring. The reaction was completed within 0.5 h. The reaction mixture was then extracted with well-degassed toluene in glovebox (15 g toluene for 1st extraction, and 10 g toluene for 2nd and 3rd extraction, respectively). The extracted toluene solution was then dried over excessive Na₂SO₄ and filtered.

10 Thus, 3.63 g white solid was obtained after toluene solvent was removed in vacuo. The white solid was identified as Cy₃P with a purity of 96% by ³¹P NMR spectroscopy.

Conversion of Cy₃P=O: > 99%

Total yield of Cy₃P: 73%

Example 2

20 Under N₂ atmosphere, 8.12 g DPPhite and 2.81 g TPPhite were loaded sequentially into a 150 mL Schlenk.

5.14 g Cy₃P=O in 44.5 g anhydrous THF, 4.35 g I₂ and 0.61 g Et₃N were then added into the above Schlenk under N₂ atmosphere, respectively.

The reaction was stirred at 25 °C under N₂ atmosphere for 63 hours. THF was then removed from the reaction mixture in vacuo. The residual slurry was thoroughly washed by MTBE for three times (15 g MTBE for 1st washing, and 10 g MTBE for 2nd and 3rd washing, respectively). As a result, the solution was removed by cannulation under N₂ and the rest solid was dried in vacuo for more than 1 hour.

30 Thus, 6.94 g pale white solid was obtained, which was identified as a mixture of [Cy₃P·HI] & [Et₃NH] by ¹H NMR and ³¹P NMR spectra.

In glovebox, a 7.44 g well-degassed 10 wt% NaOH aq. solution was added slowly into the above obtained mixture of [Cy₃P·HI] & [Et₃NH] in 15 g well-degassed H₂O under stirring. The reaction was completed within 0.5 h. The reaction mixture was then extracted with well-degassed toluene in glovebox (15 g toluene for 1st extraction, and 10 g toluene for 2nd and 3rd extraction,

respectively). The extracted toluene solution was then dried over excessive Na_2SO_4 and filtered.

Thus, a 4.07 g white solid was obtained, which was identified as Cy_3P with a purity of 96% by ^{31}P NMR spectroscopy.

5 Conversion of $\text{Cy}_3\text{P}=\text{O}$: > 99%

Yield of Cy_3P : 82%

Comparative Example 1

Under N_2 atmosphere, 8.12 g DPPhite and 2.81 g TPPhite were loaded sequentially into a 150 mL Schlenk.

10 5.14 g $\text{Cy}_3\text{P}=\text{O}$ in 44.5 g anhydrous THF, 4.35 g I_2 and 0.87 g Et_3N were was then added into the above Schlenk under N_2 atmosphere, respectively.

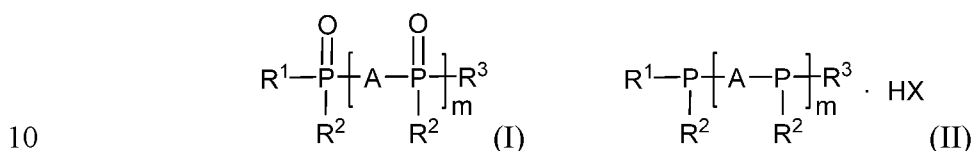
The reaction was stirred at 25°C under N_2 atmosphere for 15 hours. An aliquot of reaction mixture was taken out into 0.5 mL CDCl_3 for ^{31}P NMR analysis.

15 Unfortunately, Cy_3P was not observed by ^{31}P NMR spectrum.

CLAIMS

1. A process for the conversion of a tertiary phosphine oxide to the corresponding tertiary phosphine, comprising following steps:

- 5 (i) reacting a tertiary phosphine oxide having general formula (I) with phosphorous acid or a phosphite compound, in the presence of a halogen compound and a solvent to obtain a reaction mixture comprising a slurry comprising a tertiary phosphine hydrogen halide salt having general formula (II);



(ii) isolating the slurry obtained at step(i) from the reaction mixture;

(iii) reacting the slurry obtained at step(ii) with a base to obtain the corresponding tertiary phosphine having general formula (III);

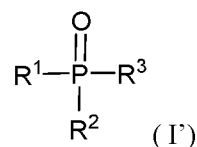


wherein:

- R^1 , R^2 and R^3 are each independently a branched, linear or cyclic $\text{C}_1\text{-C}_{20}$ alkyl or alkenyl, which is optionally interrupted by one or several heteroatoms;
- 20 - A is a linking moiety;
- m is an integer of 0 to 2;
- X is a halogen atom.

2. The process according to claim 2, wherein the tertiary phosphine oxide having general formula (I) is a compound represented by the general formula (I') as follow:

5

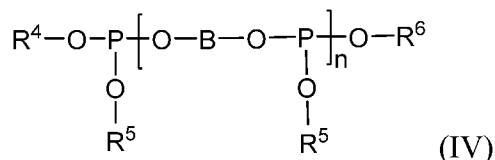


wherein R^1 , R^2 and R^3 are each independently a branched, linear or cyclic C_1 - C_{20} alkyl or alkenyl, which is optionally interrupted by one or several heteroatoms.

10 3. The process according to claim 1 or 2, wherein R^1 , R^2 and R^3 are independently R^1 , R^2 and R^3 are independently a 5-6 membered cycloalkyl, which is not interrupted by one or several heteroatoms.

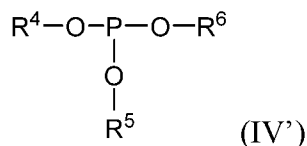
4. The process according to claim 1, wherein tertiary phosphine oxide having general formula (I) is chosen in the group consisting of
 15 trimethylphosphine oxide, dimethylethylphosphine oxide, triethylphosphine oxide, tripropylphosphine oxide, tributylphosphine oxide, tri-*tert*-butylphosphine oxide, tripentylphosphine oxide, trihexylphosphine oxide, triheptylphosphine oxide, trioctylphosphine oxide, tricyclopropylphosphine oxide, tricyclobutylphosphine oxide, tricyclopentylphosphine oxide,
 20 tricyclohexylphosphine oxide, tricycloheptylphosphine oxide, tricyclooctylphosphine oxide, ethane-1,2-diylbis(dicyclohexylphosphine oxide) and dicyclohexylmethylphosphine oxide, or any of these compounds attached to a solid and/or polymeric support.

25 5. The process according to anyone of claims 1 to 4, wherein the phosphite compound is represented by the formula (IV) as follow:



wherein R^4 , R^5 and R^6 are each independently selected from the group comprising: hydrogen, substituted or unsubstituted, branched or linear hydrocarbyl; and substituted or unsubstituted, aliphatic or aromatic carbocyclyl or heterocyclyl; B is a linking moiety; and n is an integer of from 0 to 2.

6. The process according to claim 5, wherein the phosphite compound represented by the formula (IV) is a compound represented by the general formula (IV') as follow:



10

wherein R^4 , R^5 and R^6 are each independently selected from the group comprising: hydrogen, substituted or unsubstituted, branched or linear hydrocarbyl; and substituted or unsubstituted, aliphatic or aromatic carbocyclyl or heterocyclyl; B is a linking moiety; and n is an integer of from 0 to 2.

7. The process according to claim 5 or 6, wherein R^4 , R^5 and R^6 is independently chosen in the group consisting of hydrogen atom, substituted or unsubstituted, branched or linear $\text{C}_1\text{--C}_{20}$ hydrocarbyl, substituted or unsubstituted, aliphatic or aromatic $\text{C}_3\text{--C}_{20}$ carbocyclyl, or 5-20 membered heterocyclyl.

8. The process according to claim 7, wherein R^4 , R^5 and R^6 is independently selected from the group comprising: hydrogen atom, substituted or unsubstituted $\text{C}_6\text{--C}_{20}$ aryl- $\text{C}_0\text{--C}_{20}$ alkyl.

9. The process according to claim 5, wherein the phosphite compound is chosen in the group consisting of triphenylphosphite, diphenylphosphite, phenylphosphite, diisodecylphenylphosphite, diphenyliso-decylphosphite, disooctyloctylphenylphosphite, phenyldiisodecylphosphite, tris(4-methoxyphenyl)phosphite, tri(o-tolyl)phosphite, tris(nonylphenyl)phosphite,

tetraphenyl dipropyleneglycol diphosphite, and 4,4'-isopropylidenedi-phenol C₁₂₋₁₅ alcohol phosphite.

10. The process according to anyone of claims 1 to 9, wherein the phosphite compound is present in an amount from 1 to 10 molar equivalent
5 phosphite of the phosphite compound to the phosphine oxide of the tertiary phosphine oxide having general formula (I).

11. The process according to anyone of claims 1 to 10, wherein the halogen compound is selected from the group comprising: fluorine (F₂), chlorine (Cl₂), bromine (Br₂), iodine (I₂), iodine monochloride (ICl), iodine monobromide
10 (IBr), heterocyclyl halides, haloalkanes, phosphine dihalides, and/or any trialkyl, cycloalkyl or aryl analogues thereof.

12. The process according to anyone of claims 1 to 11, wherein the halogen compound is present in an amount from 0.1 to 1.2 molar equivalents of the tertiary phosphine oxide having general formula (I).

13. The process according to anyone of claims 1 to 12, wherein the
15 reaction in step(i) is carried out in presence of an anhydrous aprotic polar solvent.

14. The process according to anyone of claims 1 to 12, wherein the reaction medium in step(i) comprises water.

15. The process according to claim 14, wherein the reaction medium in
20 step(i) comprises water with a molar ratio of water to the tertiary phosphine oxide having general formula (I) ranging from 1/1 to 10/1.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CN2018/110774

A. CLASSIFICATION OF SUBJECT MATTER

C07F 9/50(2006.01)i; C07F 9/53(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07F9/-

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

VEN, CNABS, STN(REG, CAP, CASREACT):: TERTIARY, PHOSPHINE, OXIDE?, REDUC+, PHOSPHOROUS, PHOSPHITE, HALOGEN, I2, IODINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2017041723 A1 (RHODIA OPERATIONS ET AL.) 16 March 2017 (2017-03-16) Examples 1-17, pages 6-13, and claims 1-22	1-15
X	CN 102947319 A (CHROMAFORA AB) 27 February 2013 (2013-02-27) Examples 1-16	1-15
A	US 4131624 A (M & T CHEMICALS INC) 26 December 1978 (1978-12-26) The whole document	1-15
A	CN 105968137 A (UNIV SUN YET-SEN) 28 September 2016 (2016-09-28) The whole document	1-15



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

“A” document defining the general state of the art which is not considered to be of particular relevance

“E” earlier application or patent but published on or after the international filing date

“L” document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

“O” document referring to an oral disclosure, use, exhibition or other means

“P” document published prior to the international filing date but later than the priority date claimed

“T” later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

“X” document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

“Y” document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

“&” document member of the same patent family

Date of the actual completion of the international search

10 December 2018

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INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/CN2018/110774

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INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

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