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**(71) Applicant: INVISTA TECHNOLOGIES S.A R.L.** [LU/CH]; Zweigniederlassung St. Gallen, Kreuzackerstrasse 9, CH-9000 St. Gallen (CH).

**(72) Inventors: FORSYTH, Stewart**; 102 Yearsley Place, Wilmington, DE 19808 (US). **TURNER, John, Arthur**; 19 Richardson Hall, The Green, Great Ayton, Middlesbrough, Cleveland TS9 6SA (GB). **WHISTON, Keith**; 12 Hartford Road, Darlington, Durham DL3 8 EY (GB). **VOS, Thomas, E.**; 8085 Palmetto Dunes Circle, Beaumont, TX 77707-6401 (US).

**(74) Agents: COCKERTON, Bruce, Roger** et al.; Carpmaels & Ransford, One Southampton Row, London WC1B 5HA (GB).

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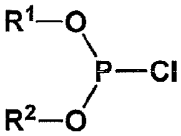
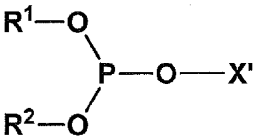
*[Continued on next page]*

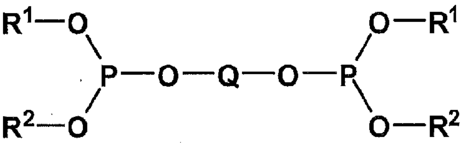
# (54) Title: METHODS FOR PRODUCING ORGANODI PHOSPHITES FROM PHOSPHOROCHLORIDITES CHARACTERIZED BY MEASURING SIDE- PRODUCT LEVELS TO DETERMINE FURTHER ADDITIONS



**Structure II**



**Structure I'**



**Structure I**

**(57) Abstract**: Claimed is a process for producing a phosphorus-containing ligand, preferably a diphosphite ligand structure (DLS) such as structure I. The method includes contacting a phosphorochloridite (structure II) with a compound having the structure X-OH (which can be a bisaryl compound), and a tertiary organic amine to provide structure I' and as prefered embodiment structure I.

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# METHODS FOR PRODUCING ORGANODIPHOSPHITES FROM PHOSPHOROCHLORIDITES CHARACTERIZED BY MEASURING SIDE-PRODUCT LEVELS TO DETERMINE FURTHER ADDITIONS

## FIELD OF THE INVENTION

**[0001]** The invention relates to a method for the synthesis of a phosphorus-containing ligand structure.

## BACKGROUND OF THE INVENTION

**[0002]** A key intermediate in the production of nylon is adiponitrile (ADN). ADN is commercially produced via hydrocyanation of 1,3-butadiene and 3-pentenenitrile (3PN) in the presence of a catalyst including nickel(0) and phosphite ligand. The phosphite ligand used commercially is a monodentate phosphite, such as a triarylphosphite, that forms nickel-ligand complexes serving as catalyst precursors for the reactions. Although useful, monodentate phosphites can result in relatively low catalyst activity and relatively high nickel consumption.

**[0003]** Recently, significant improvements in nickel catalyst activity and yield to 3PN and ADN have been realized by using catalysts including nickel(0) and bidentate phosphites as ligands. Bidentate phosphite ligands, in general, contain two phosphorus donor atoms that can form cyclic chelate structures with a single transition metal.

**[0004]** Bidentate phosphites of the general structure $(RO)_2P(OZO)P(OR)_2$, also referred to as diphosphites herein, are of special interest. Traditionally, such diphosphites can be synthesized by preparing a phosphorochloridite, $(RO)_2PCl$, from the reaction of $PCl_3$ with ROH in the presence of a tertiary organic amine. Then in a subsequent reaction, a difunctional alcohol, such as HO-Z-OH, can react with the phosphorochloridite in the presence of additional tertiary organic amine, giving $(RO)_2P(OZO)P(OR)_2$. The tertiary organic amine can neutralize the HCl co-product in both reaction steps through the formation of a tertiary organic amine hydrogen chloride salt. The nature of the ROH and the HO-Z-OH as well as the conditions chosen for each reaction step can influence the selectivity to the desired products.

**[0005]** U.S. Patent No. 5,235,113 and WO 96/22968, for example, disclose the synthesis of diphosphites. U.S. Patent No. 5,235,113 discloses a process for the preparation of a diphosphite of structure $(RO)_2P(OAO)P(OR)_2$ where A is biphenyl and R is 3,6-di-t-butyl-2-naphthyl. WO 96/22968 discloses syntheses of multidentate phosphite compounds of the type $(ArO)_2P(OZO)P(OAr)_2$, where Ar and Z are substituted or unsubstituted aryl groups.

[0006] U.S. Patent No. 6,069,267 provides a process for the preparation of organodiphosphites of the general formula $(R^1O)_2P(OZO)P(OR^1)_2$, wherein $R^1$ and Z are different substituted or unsubstituted aryl groups

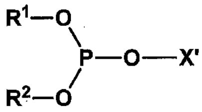
[0007] WO 2004/050588 discloses that low temperature and viscosity of the product mixture below 0°C, for example between 0°C and –20°C, add significantly to operating cost and process complexity.

[0008] WO 2004/091780 also describes a process for preparing a crude ligand mixture including bidentate phosphite ligands of the structural formula $(R^1O)_2P(OZO)P(OR^1)_2$ by contacting a first reaction product including $(R^1O)_2PCl$ at a temperature between about –25°C and about +35°C with about one half molar equivalent of HO-Z-OH in the presence of an organic base.

[0009] WO 2010/123743 and WO 2010/123747 describe examples of methods for making organodiphosphites.

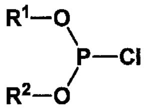
## SUMMARY OF THE INVENTION

[0010] Various embodiments of the present invention provide a method for producing a phosphorus-containing ligand structure having the following chemical structure



**Structure I'**

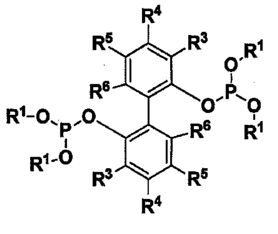
The method includes contacting a phosphorochloridite of the following structure,



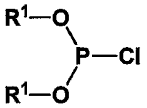
**Structure II**

with a compound having the chemical structure X-OH and a tertiary organic amine to provide a final reaction mixture including the phosphorus-containing ligand structure. The contacting includes providing a pre-determined limit for a mole percent of phosphorus present as at least one side-product in the final reaction mixture. The contacting also includes adding the X-OH to the phosphorochloridite in a first serial addition, to provide a first reaction mixture. The contacting also includes determining a mole percent of phosphorus present in the first reaction mixture as the at least one side-product. The contacting also includes using a comparison of the mole percent of phosphorus present in the first reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and an alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a second serial addition. The contacting also includes adding the second serial addition to the first reaction mixture, including a compound selected from the group consisting of the X-OH, water, or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide a second reaction mixture. The contacting also either includes performing third addition steps, or the final reaction mixture is the second reaction mixture. The third addition steps, if performed, include optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition. The third addition steps, if performed, include optionally determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product. The third addition steps, if performed, also include adding the third serial addition to the second reaction mixture, including a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture. In this paragraph, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; $R^1$ and $R^2$ are bridged to one another or unbridged to one another; and each of X and X' are independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, phosphitylbisaryl, phosphitylbisheteroaryl, hydroxybisaryl, hydroxybisheteroaryl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups.

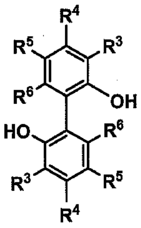
**[0011]** Various embodiments of the present invention provide a method for producing a diphosphite ligand structure (DLS) having the following structure,



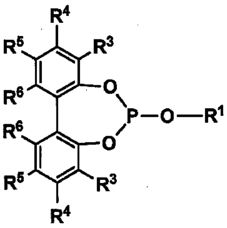
The method includes contacting a phosphorochloridite having the following structure,



with a bisaryl compound having the following structure,

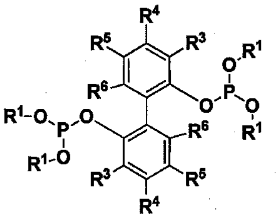


and a tertiary organic amine to provide a final reaction mixture including the diphosphite. The contacting includes providing a pre-determined limit for the mole percent of phosphorus present as C-phite ligand structure (CLS), having the chemical structure shown below, in the final reaction mixture

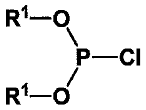


The contacting also includes adding the bisaryl compound to the phosphorochloridite in a first serial addition such that the moles of phosphorochloridite added in the first addition is greater than the number of moles of the bisaryl compound added in the first addition, to provide a first reaction mixture. The contacting also includes determining the mole percent of phosphorus present in the first reaction mixture as CLS. The contacting also includes using a comparison of the mole percent of phosphorus present in the first reaction mixture as CLS to the pre-determined limit for the mole percent of phosphorus present as CLS to determine an amount of a compound selected from the group consisting of at least one of the bisaryl compound, water, and an alcohol having the chemical structure $R^1$-OH, to add in a second serial addition such that the mole percent of phosphorus present as CLS in a second reaction mixture is less than or equal to the pre-determined limit for the mole percent of phosphorus present as CLS in the final reaction mixture. The contacting also includes adding the second serial addition to the first reaction mixture, including a compound selected from the group consisting of the bisaryl compound, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the second reaction mixture. The contacting also includes either performing third addition steps, or the final reaction mixture is the second reaction mixture. The third addition steps, if performed, include optionally determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product. The third addition steps, if performed, include optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition. The third addition steps, if performed, include adding the third serial addition to the second reaction mixture, including a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture. In this paragraph, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

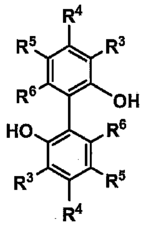
**[0012]** Various embodiments of the present invention provide a method for producing a diphosphite ligand structure (DLS) having the following structure,



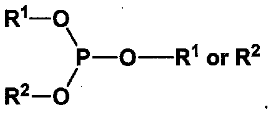
The method includes contacting a phosphorochloridite having the following structure,



with a bisaryl compound having the following structure,

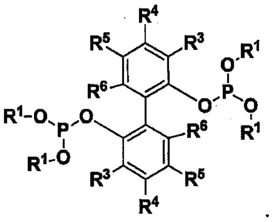


and a tertiary organic amine to provide a final reaction mixture including the diphosphite. The contacting includes providing a pre-determined limit for the mole percent of phosphorus present as T-phite ligand structure (TLS), having the chemical structure shown below, in the final reaction mixture

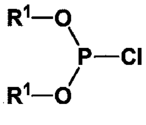


The contacting also includes adding the bisaryl compound to the phosphorochloridite in a first serial addition such that the moles of phosphorochloridite added in the first addition is greater than the number of moles of biaryl added in the first addition, to provide a first reaction mixture. The contacting also includes determining the mole percent of phosphorus present in the first reaction mixture as TLS. The contacting also includes using a comparison of the mole percent of phosphorus present in the first reaction mixture as TLS to the pre-determined limit for the mole percent of phosphorus present as TLS to determine an amount of a compound selected from the group consisting of the bisaryl compound, water, and an alcohol having the chemical structure $R^1$-OH, to add in a second serial addition such that the mole percent of phosphorus present as TLS in a second reaction mixture is less than or equal to the pre-determined limit for the mole percent of phosphorus present as TLS in the final reaction mixture. The contacting also includes adding the second serial addition to the first reaction mixture, including a compound selected from the group consisting of the bisaryl compound, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the second reaction mixture. The contacting also includes either performing third addition steps, or the final reaction mixture is the second reaction mixture. The third addition steps, if performed, include optionally determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product. The third addition steps, if performed, also include optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition. The third addition steps, if performed, also include adding the third serial addition to the second reaction mixture, including a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture. In this paragraph, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; and each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

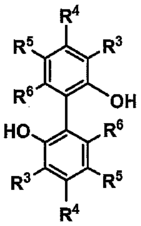
**[0013]** Various embodiments of the present invention provide a method for producing a diphosphite ligand structure (DLS) having the following structure,



The method includes contacting a phosphorochloridite having the following structure,

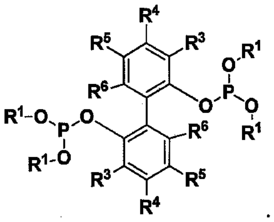


with a bisaryl compound having the following structure,

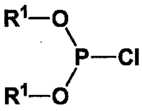


and a tertiary organic amine to provide a final reaction mixture including the diphosphite. The contacting includes providing a pre-determined limit for the mole percent of phosphorus present as a ligand hydrolysis product (LHP) in the final reaction mixture. The LHP includes at least one product derived by a process including hydrolysis of the DLS or of the phosphorochloridite; hydrolysis of a product derived from the DLS or from the phosphorochloridite; or reaction of the hydrolysis product of the DLS or of the phosphorochloridite, or reaction of the hydrolysis product of a product derived from the DLS or from the phosphorochloridite. The contacting includes adding the bisaryl compound to the phosphorochloridite in a first serial addition such that the moles of phosphorochloridite added in the first addition is greater than the number of moles of biaryl added in the first addition, to provide a first reaction mixture. The contacting includes determining the mole percent of phosphorus present in the first reaction mixture as LHP. The contacting includes using a comparison of the mole percent of phosphorus present in the first reaction mixture as LHP to the pre-determined limit for the mole percent of phosphorus present as LHP to determine an amount of a compound selected from the group consisting of the bisaryl compound, water, and an alcohol having the chemical structure $R^1$-OH, to add in a second serial addition such that the mole percent of phosphorus present as LHP in a second reaction mixture is less than or equal to the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture. The contacting includes adding the second serial addition to the first reaction mixture, including a compound selected from the group consisting of the bisaryl compound, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the second reaction mixture. The contacting also includes either performing third addition steps or the final reaction mixture is the second reaction mixture. The third addition steps, if performed, include optionally determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product. The third addition steps, if performed, include optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition. The third addition steps, if performed, also include adding the third serial addition to the second reaction mixture, including a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture. In this paragraph, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; and each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

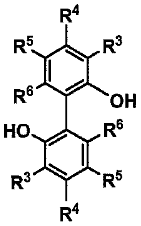
**[0014]** Various embodiments of the present invention provide a method for producing a diphosphite ligand structure (DLS) having the following structure,



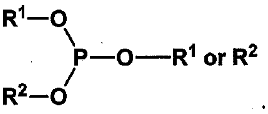
The method includes contacting a phosphorochloridite having the following structure,



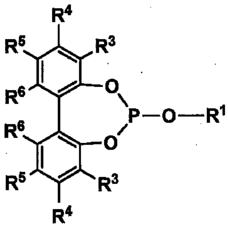
with a bisaryl compound having the following structure,



and a tertiary organic amine to provide a final reaction mixture including the diphosphite. The contacting includes providing a pre-determined limit for the mole percent of phosphorus present as T-phite ligand structure (TLS), having the chemical structure shown below, in the final reaction mixture



The contacting also includes providing a pre-determined limit for the mole percent of phosphorus present as C-phite ligand structure (CLS), having the chemical structure shown below, in the final reaction mixture



The contacting also includes providing a pre-determined limit for the mole percent of phosphorus present as a ligand hydrolysis product (LHP) in the final reaction mixture. LHP includes at least one product derived by a process including hydrolysis of the DLS or of the phosphorochloridite; hydrolysis of a product derived from the DLS or from the phosphorochloridite; or reaction of the hydrolysis product of the DLS or of the phosphorochloridite, or reaction of the hydrolysis product of a product derived from the DLS or from the phosphorochloridite. The contacting also includes providing a pre-determined goal for a conversion of phosphorochloridite in the first reaction mixture. The contacting also includes adding the bisaryl compound to the phosphorochloridite in a first serial addition to provide a first reaction mixture, wherein the amount of bisaryl compound added is sufficient to cause the percent conversion of the phosphorochloridite in the first reaction mixture to be equal to or greater than the pre-determined goal for a conversion of the phosphorochloridite in the first reaction mixture. The contacting also includes determining the mole percent of phosphorus present in the first reaction mixture as TLS. The contacting also includes determining the mole percent of phosphorus present in the first reaction mixture as CLS. The contacting also includes determining the percent conversion of the phosphorochloridite in the first reaction mixture. If in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition includes water. If in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition includes the alcohol having the chemical structure $R^1$-OH or $R^2$-OH. If in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction product is less than the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture, then second serial addition includes the bisaryl compound, wherein the quantity of the bisaryl compound to add in the second serial addition is determined using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of the bisaryl compound to add in the second serial addition. Using the comparison to determine the amount of bisaryl compound to add in the second serial addition includes using at least one selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range in combination with the determined mole percents of TLS and CLS in the first reaction mixture to forecast a maximum percent conversion of phosphorochloridite such that at the forecasted percent conversion in the second reaction mixture the percent of phosphorus present as CLS in the second reaction mixture is less than the pre-determined limit for the percent of phosphorus present as CLS in the final reaction mixture. Using the comparison to determine the amount of bisaryl compound to add in the second serial addition also includes setting a pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to the forecasted maximum percent conversion of the phosphorochloridite. The contacting also includes adding the second serial addition to the first reaction mixture, including a compound selected from the group consisting of the bisaryl compound, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the second reaction mixture, wherein if bisaryl compound is added in the second serial addition then the amount of the bisaryl compound in the second serial addition is sufficient to cause the percent conversion of the phosphorochloridite in the second reaction mixture to be about equal to the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture. The contacting also includes either performing third addition steps, or the final reaction mixture is the second reaction mixture. If the final reaction mixture is the second reaction mixture, the quantities of the one of more compound added in the second addition are such that conversion of the phosphorochloridite in the final reaction mixture is about 100%. Third addition steps, if performed, include optionally determining a mole percent of phosphorus present in the second reaction mixture as at least one side-product. Third addition steps, if performed, include optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of water and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition. Third addition steps, if performed, also include adding the third serial addition to the second reaction mixture to provide the final reaction mixture, wherein the quantities of the one or more compounds added in the third addition are such that the conversion of the phosphorochloridite in the final reaction mixture is about 100%. In this paragraph, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; and each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

**[0015]** The present invention provides certain advantages over other methods of producing a phosphorus-containing ligand, including a diphosphite-containing ligand structure (DLS). In some embodiments, the phosphorus-containing ligand or DLS is generated at higher yield than other methods. In various embodiments, the phosphorus-containing ligand is generated with smaller amounts of impurities than other methods, for example the DLS can be generated with smaller amounts of TLS or CLS than other methods. In some embodiments, in the final product mixture the phosphorus-containing ligand can be generated with smaller amounts of hydrolysis products than other methods. For example, in the final product mixture the DLS can be generated with smaller amounts of ligand hydrolysis products (LHPs) than other methods. In some embodiments, the phosphorus-containing ligand can be generated with a more highly controlled amount of impurities and hydrolysis products than other methods. For example, the DLS can be generated with a more highly controlled amount of TLS, CLS, or LHPs than other methods. In some embodiments, in the final product mixture impurities or hydrolysis products are present within specified limits for maximum concentration while the yield of the phosphorus-containing ligand is higher than that of other methods that can keep impurities or hydrolysis products within similar limits. For example, in the final product mixture TLS, CLS, and LHPs can be present within specified limits for maximum concentration while the yield of the DLS can be higher than that of other methods that can keep TLS, CLS and LHP concentrations within similar limits. In some embodiments, the final product mixture containing the phosphorus-containing ligand has low enough concentrations of impurities or hydrolysis products that the final product mixture can be used to generate a complex that can function more efficiently as a catalyst than the catalyst formed from the final product mixture of other phosphorus-containing ligand synthesis methods. For example, the final product mixture containing the DLS can have low enough concentrations of TLS, CLS, or LHPs that the final product mixture can be used to generate a nickel(0)-DLS complex that can function more efficiently as a hydrocyanation catalyst than the nickel(0)-DLS complex formed from the final product mixture of other DLS synthesis methods. In some embodiments, the final product mixture can have low enough concentrations of impurities or hydrolysis products that it can be used to generate a catalyst that can efficiently catalyze a particular reaction, while the overall yield of the phosphorus-containing ligand can be higher than that of other methods used to make final reaction mixtures that include the phosphorus-containing ligand and that can generate a catalyst as efficient for catalyzing the particular reaction. For example, the final product mixture can have low enough concentrations of TLS, CLS, or LHPs that it can be used to generate a nickel(0)-DLS complex that can function efficiently as a hydrocyanation catalyst, while the overall yield of DLS can be higher than that of other methods used to make DLS-containing final product mixtures that can form nickel(0)-DLS complexes efficient for catalyzing hydrocyanation reactions. In various embodiments, the method can be consistently repeated to produce final reaction mixtures with impurity levels within specification limits. In some examples, the method can be consistently repeated to produce final reaction mixtures with highly consistent impurity levels and yields of the phosphorus-containing ligand. In some examples, the method can be consistently repeated to produce final reaction mixtures with highly consistent levels of the CLS side-product, within specification limits. In some embodiments, the phosphorus-containing ligand or a catalyst complex made from the ligand can be efficiently recycled after use in a hydrocyanation reaction while maintaining a higher catalytic efficiency than phosphorus-containing ligands or complexes made therefrom made by other methods. Various embodiments of the present invention satisfy a need for a simple and selective process for preparing a phosphorus-containing ligand, including a DLS, to meet predetermined purity specifications, including for use as components of hydrocyanation catalysts. While obtaining high selectivities for formation of phosphorus-containing ligands such as DLS, some embodiments of the present invention provide a method for overcoming temperature limitations of other methods, such as those identified in U.S. Patent No. 6,069,267 and WO 2004/050588.

## DETAILED DESCRIPTION OF THE INVENTION

**[0016]** Reference will now be made in detail to certain claims of the disclosed subject matter. While the disclosed subject matter will be described in conjunction with the enumerated claims, it will be understood that they are not intended to limit the disclosed subject matter to those claims. On the contrary, the disclosed subject matter is intended to cover all alternatives, modifications, and equivalents, which can be included within the scope of the presently disclosed subject matter as defined by the claims.

**[0017]** References in the specification to "one embodiment," "an embodiment," "an example embodiment," etc., indicate that the embodiment described can include a particular feature, structure, or characteristic, but every embodiment may not necessarily include the particular feature, structure, or characteristic. Moreover, such phrases are not necessarily referring to the same embodiment. Further, when a particular feature, structure, or characteristic is described in connection with an embodiment, it is submitted that it is within the knowledge of one skilled in the art to affect such feature, structure, or characteristic in connection with other embodiments whether or not explicitly described.

**[0018]** In this document, the terms "a" or "an" are used to include one or more than one and the term "or" is used to refer to a nonexclusive "or" unless otherwise indicated. In addition, it is to be understood that the phraseology or terminology employed herein, and not otherwise defined, is for the purpose of description only and not of limitation. Any use of section headings is intended to aid reading of the document and is not to be interpreted as limiting; information that is relevant to a section heading can occur within or outside of that particular section. Furthermore, all publications, patents, and patent documents referred to in this document are incorporated by reference herein in their entirety, as though individually incorporated by reference. In the event of inconsistent usages between this document and those documents so incorporated by reference, the usage in the incorporated reference should be considered supplementary to that of this document; for irreconcilable inconsistencies, the usage in this document controls.

**[0019]** In the methods of manufacturing described herein, the steps can be carried out in any order without departing from the principles of the invention, except when a temporal or operational sequence is explicitly recited. Recitation in a claim to the effect that first a step is performed, then several other steps are subsequently performed, shall be taken to mean that the first step is performed before any of the other steps, but the other steps can be performed in any suitable sequence, unless a sequence is further recited within the other steps. For example, claim elements that recite "Step A, Step B, Step C, Step D, and Step E" shall be construed to mean step A is carried out first, step E is carried out last, and steps B, C, and D can be carried out in any sequence between steps A and E, and that the sequence still falls within the literal scope of the claimed process. A given step or sub-set of steps can also be repeated, or carried out simultaneously with other steps. In another example, claim elements that recite "Step A, Step B, Step C, Step D, and Step E" can be construed to mean Step A is carried out first, Step B is carried out next, Step C is carried out next, Step D is carried out next, and Step E is carried out last.

**[0020]** Furthermore, specified steps can be carried out concurrently unless explicit claim language recites that they be carried out separately. For example, a claimed step of doing X and a claimed step of doing Y can be conducted simultaneously within a single operation, and the resulting process will fall within the literal scope of the claimed process.

Definitions

**[0021]** The singular forms "a," "an" and "the" can include plural referents unless the context clearly dictates otherwise.

**[0022]** The term "about" can allow for a degree of variability in a value or range, for example, within 10%, within 5%, or within 1% of a stated value or of a stated limit of a range. When a range or a list of sequential values is given, unless otherwise specified any value within the range or any value between the given sequential values is also disclosed.

**[0023]** The term "organic group" as used herein refers to but is not limited to any carbon-containing functional group. For example, an oxygen-containing group such as alkoxy groups, aryloxy groups, aralkyloxy groups, oxo(carbonyl) groups, carboxyl groups including carboxylic acids, carboxylates, and carboxylate esters; a sulfur-containing group such as alkyl and aryl sulfide groups; and other heteroatom-containing groups. Non-limiting examples of organic groups include OR', $OC(O)N(R')_2$, CN, $CF_3$, $OCF_3$, R', C(O), methylenedioxy, ethylenedioxy, $N(R')_2$, SR', SOR', $SO_2R'$, $SO_2N(R')_2$, $SO_3R'$, C(O)R', C(O)C(O)R', $C(O)CH_2C(O)R'$, C(S)R', C(O)OR', OC(O)R', $C(O)N(R')_2$, $OC(O)N(R')_2$, $C(S)N(R')_2$, $(CH_2)_{0-2}N(R')C(O)R'$, $(CH_2)_{0-2}N(R')N(R')_2$, N(R')N(R')C(O)R', N(R')N(R')C(O)OR', $N(R')N(R')CON(R')_2$, $N(R')SO_2R'$, $N(R')SO_2N(R')_2$, N(R')C(O)OR', N(R')C(O)R', N(R')C(S)R', $N(R')C(O)N(R')_2$, $N(R')C(S)N(R')_2$, N(COR')COR', N(OR')R', $C(=NH)N(R')_2$, C(O)N(OR')R', or C(=NOR')R' wherein R' can be hydrogen (in examples that include other carbon atoms) or a carbon-based moiety, and wherein the carbon-based moiety can itself be further substituted; for example, wherein R' can be hydrogen (in examples that include other carbon atoms), alkyl, acyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, or heteroarylalkyl, wherein any alkyl, acyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, or heteroarylalkyl, or R' can be independently mono- or multi-substituted with J; or wherein two R' groups bonded to a nitrogen atom or to adjacent nitrogen atoms can together with the nitrogen atom or atoms form a heterocyclyl, which can be mono- or independently multi-substituted with J. Examples of organic groups include linear and/or branched groups such as alkyl groups, fully or partially halogen-substituted haloalkyl groups, alkenyl groups, alkynyl groups, aromatic groups, acrylate functional groups, and methacrylate functional groups; and other organic functional groups such as ether groups, cyanate ester groups, ester groups, carboxylate salt groups, and masked isocyano groups. Examples of organic groups include, but are not limited to, alkyl groups such as methyl, ethyl, propyl, isopropyl, n-butyl, s-butyl, and t-butyl groups, acrylate functional groups such as acryloyloxypropyl groups and methacryloyloxypropyl groups; alkenyl groups such as vinyl, allyl, and butenyl groups; alkynyl groups such as ethynyl and propynyl groups; aromatic groups such as phenyl, tolyl, and xylyl groups; cyanoalkyl groups such as cyanoethyl and cyanopropyl groups; halogenated hydrocarbon groups such as 3,3,3-trifluoropropyl, 3-chloropropyl, dichlorophenyl, and 6,6,6,5,5,4,4,3,3-nonafluorohexyl groups; alkenyloxypoly(oxyalkyene) groups such as allyloxy(polyoxyethylene), allyloxypoly(oxypropylene), and allyloxy-poly(oxypropylene)-co-poly(oxyethylene) groups; alkyloxypoly(oxyalkyene) groups such as propyloxy(polyoxyethylene), propyloxypoly(oxypropylene), and propyloxy-poly(oxypropylene)-co-poly(oxyethylene) groups; halogen substituted alkyloxypoly(oxyalkyene) groups such as perfluoropropyloxy(polyoxyethylene), perfluoropropyloxypoly(oxypropylene), and perfluoropropyloxy-poly(oxypropylene)-co-poly(oxyethylene) groups; alkoxy groups such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, and ethylhexyloxy groups; aminoalkyl groups such as 3-aminopropyl, 6-aminohexyl, 11-aminoundecyl, 3-(N-allylamino)propyl, N-(2-aminoethyl)-3-aminopropyl, N-(2-aminoethyl)-3-aminoisobutyl, p-aminophenyl, 2-ethylpyridine, and 3-propylpyrrole groups; epoxyalkyl groups such as 3-glycidoxypropyl, 2-(3,4,-epoxycyclohexyl)ethyl, and 5,6-epoxyhexyl groups; ester functional groups such as actetoxyethyl and benzoyloxypropyl groups; hydroxy functional groups such as 2-hydroxyethyl groups; masked isocyanate functional groups such as propyl-t-butylcarbamate, and propylethylcarbamate groups; aldehyde functional groups such as undecanal and butyraldehyde groups; anhydride functional groups such as 3-propyl succinic anhydride and 3-propyl maleic anhydride groups; and metal salts of carboxylic acids such as the zinc, sodium, or potassium salts of 3-carboxypropyl and 2-carboxyethyl.

**[0024]** The term “substituted” as used herein refers to an organic group as defined herein or molecule in which one or more bonds to a hydrogen atom contained therein are replaced by one or more bonds to a non-hydrogen atom. The term “functional group” or “substituent” as used herein refers to a group that can be or is substituted onto a molecule, or onto an organic group. Examples of substituents or functional groups include, but are not limited to, a halogen (e.g., F, Cl, Br, and I); an oxygen atom in groups such as hydroxyl groups, alkoxy groups, aryloxy groups, aralkyloxy groups, oxo(carbonyl) groups, carboxyl groups including carboxylic acids, carboxylates, and carboxylate esters; a sulfur atom in groups such as thiol groups, alkyl and aryl sulfide groups, sulfoxide groups, sulfone groups, sulfonyl groups, and sulfonamide groups; a nitrogen atom in groups such as amines, hydroxylamines, nitriles, nitro groups, N-oxides, hydrazides, azides, and enamines; and other heteroatoms in various other groups. Non-limiting examples of substituents J that can be bonded to a substituted carbon (or other) atom include F, Cl, Br, I, OR', $OC(O)N(R')_2$, CN, NO, $NO_2$, $ONO_2$, azido, $CF_3$, $OCF_3$, R', O (oxo), S (thiono), C(O), S(O), methylenedioxy, ethylenedioxy, $N(R')_2$, SR', SOR', $SO_2R'$, $SO_2N(R')_2$, $SO_3R'$, C(O)R', C(O)C(O)R', $C(O)CH_2C(O)R'$, C(S)R', C(O)OR', OC(O)R', $C(O)N(R')_2$, $OC(O)N(R')_2$, $C(S)N(R')_2$, $(CH_2)_{0-2}N(R')C(O)R'$, $(CH_2)_{0-2}N(R')N(R')_2$, N(R')N(R')C(O)R', N(R')N(R')C(O)OR', $N(R')N(R')CON(R')_2$, $N(R')SO_2R'$, $N(R')SO_2N(R')_2$, N(R')C(O)OR', N(R')C(O)R', N(R')C(S)R', $N(R')C(O)N(R')_2$, $N(R')C(S)N(R')_2$, N(COR')COR', N(OR')R', $C(=NH)N(R')_2$, C(O)N(OR')R', or C(=NOR')R' wherein R’ can be hydrogen or a carbon-based moiety, and wherein the carbon-based moiety can itself be further substituted; for example, wherein R’ can be hydrogen, alkyl, acyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, or heteroarylalkyl, wherein any alkyl, acyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, or heteroarylalkyl or R’ can be independently mono- or multi-substituted with J; or wherein two R’ groups bonded to a nitrogen atom or to adjacent nitrogen atoms can together with the nitrogen atom or atoms form a heterocyclyl, which can be mono- or independently multi-substituted with J.

**[0025]** The term “alkyl” as used herein refers to straight chain and branched alkyl groups and cycloalkyl groups having from 1 to about 20 carbon atoms, and typically from 1 to 12 carbons or, in some embodiments, from 1 to 8 carbon atoms. Examples of straight chain alkyl groups include those with from 1 to 8 carbon atoms such as methyl, ethyl, n-propyl, n-butyl, n-pentyl, n-hexyl, n-heptyl, and n-octyl groups. Examples of branched alkyl groups include, but are not limited to, isopropyl, iso-butyl, sec-butyl, t-butyl, neopentyl, isopentyl, and 2,2-dimethylpropyl groups. As used herein, the term "alkyl" encompasses n-alkyl, isoalkyl, and anteisoalkyl groups as well as other branched chain forms of alkyl. Representative substituted alkyl groups can be substituted one or more times with any of the groups listed herein, for example, amino, hydroxy, cyano, carboxy, nitro, thio, alkoxy, and halogen groups.

**[0026]** The term "alkenyl" as used herein refers to straight and branched chain and cyclic alkyl groups as defined herein, except that at least one double bond exists between two carbon atoms. Thus, alkenyl groups have from 2 to about 20 carbon atoms, and typically from 2 to 12 carbons or, in some embodiments, from 2 to 8 carbon atoms. Examples include, but are not limited to vinyl, $-CH=CH(CH_3)$, $-CH=C(CH_3)_2$, $-C(CH_3)=CH_2$, $-C(CH_3)=CH(CH_3)$, $-C(CH_2CH_3)=CH_2$, cyclohexenyl, cyclopentenyl, cyclohexadienyl, butadienyl, pentadienyl, and hexadienyl among others.

**[0027]** The term "alkynyl" as used herein refers to straight and branched chain alkyl groups, except that at least one triple bond exists between two carbon atoms. Thus, alkynyl groups have from 2 to about 20 carbon atoms, and typically from 2 to 12 carbons or, in some embodiments, from 2 to 8 carbon atoms. Examples include, but are not limited to $-C\equiv CH$, $-C\equiv C(CH_3)$, $-C\equiv C(CH_2CH_3)$, $-CH_2C\equiv CH$, $-CH_2C\equiv C(CH_3)$, and $-CH_2C\equiv C(CH_2CH_3)$ among others.

**[0028]** The term "acyl" as used herein refers to a group containing a carbonyl moiety wherein the group is bonded via the carbonyl carbon atom. The carbonyl carbon atom is also bonded to another carbon atom, which can be part of an alkyl, aryl, aralkyl cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl group or the like. In the special case wherein the carbonyl carbon atom is bonded to a hydrogen, the group is a "formyl" group, an acyl group as the term is defined herein. An acyl group can include 0 to about 12-20 additional carbon atoms bonded to the carbonyl group. An acyl group can include double or triple bonds within the meaning herein. An acryloyl group is an example of an acyl group. An acyl group can also include heteroatoms within the meaning here. A nicotinoyl group (pyridyl-3-carbonyl) group is an example of an acyl group within the meaning herein. Other examples include acetyl, benzoyl, phenylacetyl, pyridylacetyl, cinnamoyl, and acryloyl groups and the like. When the group containing the carbon atom that is bonded to the carbonyl carbon atom contains a halogen, the group is termed a "haloacyl" group. An example is a trifluoroacetyl group.

**[0029]** The term "cycloalkyl" as used herein refers to cyclic alkyl groups such as, but not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl groups. In some embodiments, the cycloalkyl group can have 3 to about 8-12 ring members, whereas in other embodiments the number of ring carbon atoms range from 3 to 4, 5, 6, or 7. Cycloalkyl groups further include polycyclic cycloalkyl groups such as, but not limited to, norbornyl, adamantyl, bornyl, camphenyl, isocamphenyl, and carenyl groups, and fused rings such as, but not limited to, decalinyl, and the like. Cycloalkyl groups also include rings that are substituted with straight or branched chain alkyl groups as defined herein. Representative substituted cycloalkyl groups can be mono-substituted or substituted more than once, such as, but not limited to, 2,2-, 2,3-, 2,4- 2,5- or 2,6-disubstituted cyclohexyl groups or mono-, di- or tri-substituted norbornyl or cycloheptyl groups, which can be substituted with, for example, amino, hydroxy, cyano, carboxy, nitro, thio, alkoxy, and halogen groups. The term "cycloalkenyl" alone or in combination denotes a cyclic alkenyl group.

**[0030]** The term "aryl" as used herein refers to cyclic aromatic hydrocarbons that do not contain heteroatoms in the ring. Thus aryl groups include, but are not limited to, phenyl, azulenyl, heptalenyl, biphenyl, indacenyl, fluorenyl, phenanthrenyl, triphenylenyl, pyrenyl, naphthacenyl, chrysenyl, biphenylenyl, anthracenyl, and naphthyl groups. In some embodiments, aryl groups contain about 6 to about 14 carbons in the ring portions of the groups. Aryl groups can be unsubstituted or substituted, as defined herein. Representative substituted aryl groups can be mono-substituted or substituted more than once, such as, but not limited to, 2-, 3-, 4-, 5-, or 6-substituted phenyl or 2-8 substituted naphthyl groups, which can be substituted with carbon or non-carbon groups such as those listed herein

**[0031]** The term "heteroaryl" as used herein refers to aromatic ring compounds containing 5 or more ring members, of which, one or more is a heteroatom such as, but not limited to, N, O, and S; for instance, heteroaryl rings can have 5 to about 8-12 ring members. A heteroaryl group is a variety of a heterocyclyl group that possesses an aromatic electronic structure. A heteroaryl group designated as a $C_2$-heteroaryl can be a 5-ring with two carbon atoms and three heteroatoms, a 6-ring with two carbon atoms and four heteroatoms and so forth. Likewise a $C_4$-heteroaryl can be a 5-ring with one heteroatom, a 6-ring with two heteroatoms, and so forth. The number of carbon atoms plus the number of heteroatoms sums up to equal the total number of ring atoms. Heteroaryl groups include, but are not limited to, groups such as pyrrolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isoxazolyl, thiazolyl, pyridinyl, thiophenyl, benzothiophenyl, benzofuranyl, indolyl, azaindolyl, indazolyl, benzimidazolyl, azabenzimidazolyl, benzoxazolyl, benzothiazolyl, benzothiadiazolyl, imidazopyridinyl, isoxazolopyridinyl, thianaphthalenyl, purinyl, xanthinyl, adeninyl, guaninyl, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, quinoxalinyl, and quinazolinyl groups. Heteroaryl groups can be unsubstituted, or can be substituted with groups as is discussed herein. Representative substituted heteroaryl groups can be substituted one or more times with groups such as those listed herein.

**[0032]** The term “alkoxy" as used herein refers to an oxygen atom connected to an alkyl group, including a cycloalkyl group, as are defined herein. Examples of linear alkoxy groups include but are not limited to methoxy, ethoxy, propoxy, butoxy, pentyloxy, hexyloxy, and the like. Examples of branched alkoxy include but are not limited to isopropoxy, sec-butoxy, tert-butoxy, isopentyloxy, isohexyloxy, and the like. Examples of cyclic alkoxy include but are not limited to cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, and the like. An alkoxy group can include one to about 12-20 carbon atoms bonded to the oxygen atom, and can further include double or triple bonds, and can also include heteroatoms. For example, an allyloxy group is an alkoxy group within the meaning herein. A methoxyethoxy group is also an alkoxy group within the meaning herein, as is a methylenedioxy group in a context where two adjacent atoms of a structures are substituted therewith.

**[0033]** The term “amine” as used herein refers to primary, secondary, and tertiary amines having, e.g., the formula $N(group)_3$ wherein each group can independently be H or non-H, such as alkyl, aryl, and the like. Amines include but are not limited to $R-NH_2$, for example, alkylamines, arylamines, alkylarylamines; $R_2NH$ wherein each R is independently selected, such as dialkylamines, diarylamines, aralkylamines, heterocyclylamines and the like; and $R_3N$ wherein each R is independently selected, such as trialkylamines, dialkylarylamines, alkyldiarylamines, triarylamines, and the like. The term "amine" also includes ammonium ions as used herein.

**[0034]** The term "amino group” as used herein refers to a substituent of the form $-NH_2$, -NHR, $-NR_2$, $-NR_3^+$, wherein each R is independently selected, and protonated forms of each, except for -$NR_3^+$, which cannot be protonated. Accordingly, any compound substituted with an amino group can be viewed as an amine. An "amino group" within the meaning herein can be a primary, secondary, tertiary or quaternary amino group. An "alkylamino" group includes a monoalkylamino, dialkylamino, and trialkylamino group.

**[0035]** The terms “halo” or “halogen” or "halide", as used herein, by themselves or as part of another substituent mean, unless otherwise stated, a fluorine, chlorine, bromine, or iodine atom, preferably, fluorine, chlorine, or bromine.

**[0036]** The term “haloalkyl” group, as used herein, includes mono-halo alkyl groups, poly-halo alkyl groups wherein all halo atoms can be the same or different, and per-halo alkyl groups, wherein all hydrogen atoms are replaced by halogen atoms, such as fluoro. Examples of haloalkyl include trifluoromethyl, 1,1-dichloroethyl, 1,2-dichloroethyl, 1,3-dibromo-3,3-difluoropropyl, perfluorobutyl, and the like.

**[0037]** The term “monovalent” as used herein refers to a substituent connecting via a single bond to a substituted molecule. When a substituent is monovalent, such as, for example, F or Cl, it is bonded to the atom it is substituting by a single bond.

**[0038]** The term “hydrocarbon” as used herein refers to a functional group or molecule that includes carbon and hydrogen atoms. The term can also refer to a functional group or molecule that normally includes both carbon and hydrogen atoms but wherein all the hydrogen atoms are substituted with other functional groups.

**[0039]** The term “solvent” as used herein refers to a liquid that can dissolve a solid, liquid, or gas. Nonlimiting examples of solvents are organic compounds, water, alcohols, ionic liquids, and supercritical fluids.

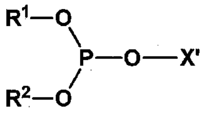
**[0040]** The term "independently selected from" as used herein refers to referenced groups being the same, different, or a mixture thereof, unless the context clearly indicates otherwise. Thus, under this definition, the phrase "$X^1$, $X^2$, and $X^3$ are independently selected from noble gases" would include the scenario where, for example, $X^1$, $X^2$, and $X^3$ are all the same, where $X^1$, $X^2$, and $X^3$ are all different, where $X^1$ and $X^2$ are the same but $X^3$ is different, and other analogous permutations.

**[0041]** The term “ligand” as used herein refers to an ion or molecule that can bind to a central metal atom (e.g. Ni(0)) to form a coordination complex (e.g. a complex between Ni(0) and DLS).

**[0042]** The phrase "stage of the contacting" for the chemical reaction of the present method has its usual meaning wherein an initial stage of the contacting is when all three reactants, phosphorochloridite, bisaryl compound, and tertiary organic amine, first come into contact and a final stage is when the reaction is terminated, for example when water is added to the reaction mixture to separate a tertiary organic amine hydrogen chloride salt from the diphosphite.

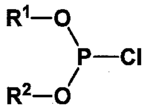
General

**[0043]** Various methods of the present invention provide a method for producing a phosphorus-containing ligand structure having the following chemical structure



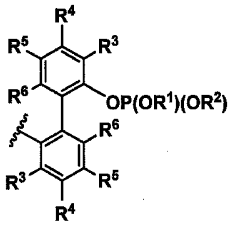
**Structure I'**

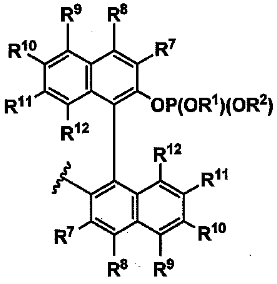
The method can include contacting a phosphorochloridite of the following structure,

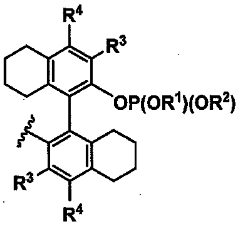


**Structure II**

with a compound having the chemical structure X-OH and a tertiary organic amine to provide a final reaction mixture including the ligand structure. The contacting includes providing a pre-determined limit for a mole percent of phosphorus present as at least one side-product in the final reaction mixture. The contacting can include adding the X-OH to the phosphorochloridite in a first serial addition, to provide a first reaction mixture. The contacting can include adding a second serial addition to the first reaction mixture, including a compound selected from the group consisting of the X-OH, water, or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide a second reaction mixture. The contacting can either includes adding a third addition or the second reaction mixture is the final reaction mixture. The third addition, if performed, can include adding a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture. In the final reaction mixture, the percentage of phosphorus present as the at least one side-product can be at or below the pre-determined limit for the mole percent of phosphorus present as at least one side-product in the final reaction mixture. In this paragraph, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; $R^1$ and $R^2$ are bridged to one another or unbridged to one another; and each of X, X', $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ is independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, phosphitylbisaryl, phosphitylbisheteroaryl, hydroxybisaryl, hydroxybisheteroaryl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups. In embodiments where X = phosphitylbisaryl, in some examples X can have a chemical structure selected from one of the following structures:



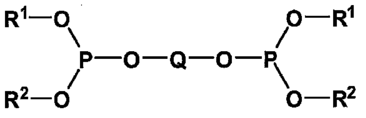




,

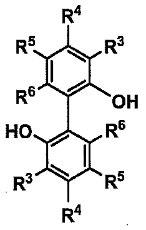
wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; $R^1$ and $R^2$ are bridged to one another or unbridged to one another; and each of $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ is independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups.

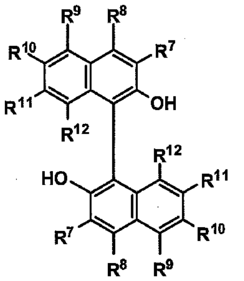
**[0044]** In various embodiments, the present invention provides a method of making a phosphorus-containing ligand, wherein the ligand structure of Structure I' can be a diphosphite ligand structure (DLS) having the chemical structure of Structure I,

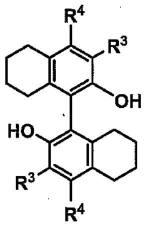


**Structure I**

wherein the X-OH can be a bisaryl compound selected from the group consisting of Structure III, Structure IV, and Structure V,







**Structure III** **Structure IV** **Structure V.**

In the Structures given in this paragraph, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; each of $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ is independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups; and O-Q-O is a divalent species of the bisaryl compound.

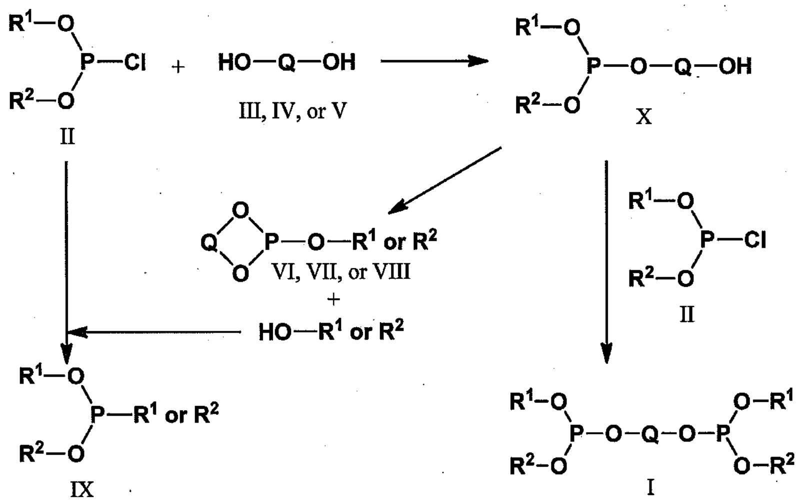
**[0045]** In the structures given herein, unless otherwise specified, X and $R^1$-$R^{12}$ are independently selected from any suitable functional group. Herein several examples are given that involve the specific embodiment of the present invention wherein a DLS is produced. However, it is to be understood that a method for DLS production is a specific embodiment of the method of the present invention, and it is not to be limited as such; rather, the present invention generally provides a method of making phosphorus-containing ligands.

**[0046]** Numerous specific examples of the method are given herein, including wherein

DLS is the phosphorus-containing ligand. These examples are not intended to limit the present invention in any way; the present invention includes a method for preparation of any suitable phosphorus-containing ligand as described herein.

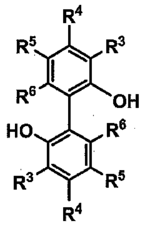
General Reaction, C-Phite Ligand Structures (CLS), T-Phite Ligand Structures (TLS), Ligand Hydrolysis Products (LHPs)

**[0047]** Scheme I illustrates a generalized reaction scheme for the specific embodiment of the method wherein the generated phosphorus-containing ligand is a DLS. One of skill in the art will readily recognize the specific embodiment shown in Scheme I as employing the compound having the structure X-OH with X = -Q-OH, and will readily be able to extrapolate a general reaction scheme using X-OH in place of HO-Q-OH from the specific reaction scheme shown. Scheme I shows a monophosphite intermediate of Structure X and monodentate triorganophosphite co-products, both cyclic and acyclic, of C-phite ligand structures (CLS) having Structures VI, VII, and VIII, and also of T-phite ligand structures (TLS) having Structure IX, respectively. $R^1$ and $R^2$ can be the same or different, substituted or unsubstituted, monovalent aryl groups. For example, $R^1$ and $R^2$ can be substituted or unsubstituted phenyl, naphthyl, anthracenyl, and phenanthrenyl groups.

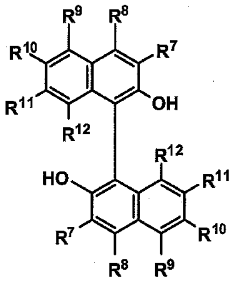


Scheme I

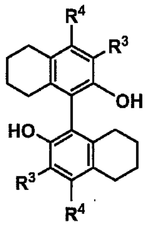
**[0048]** The bisaryl compound HO-Q-OH can have the following structures,



**Structure III**



**Structure IV**



**Structure V**

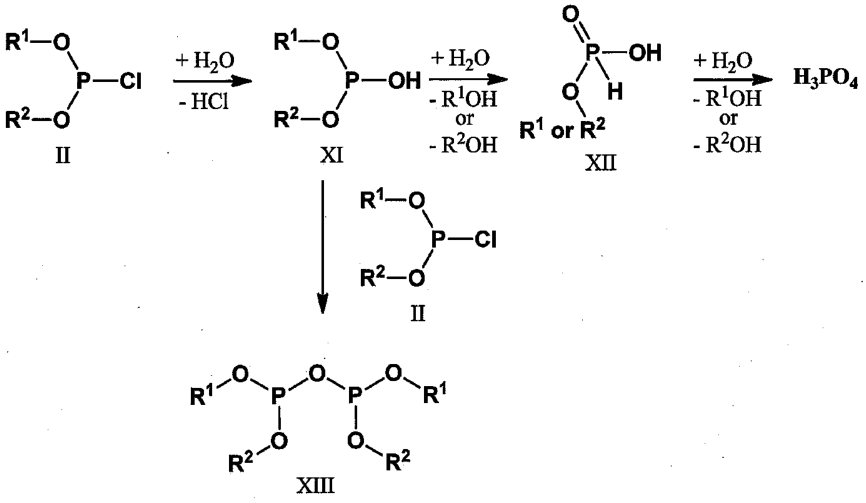
wherein each of $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ can be any suitable functional group. In one example, $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ are independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups; and O-Q-O is a divalent species of the bisaryl compound. In one example, $R^3$ to $R^{12}$ can be linear, branched, and cyclic $C_1$ to $C_{18}$ alkyl; substituted or unsubstituted $C_6$ to $C_{18}$ aryl; substituted or unsubstituted $C_6$ to $C_{18}$ aryloxy; linear, branched, and cyclic $C_1$ to $C_{18}$ alkyloxy; linear and branched $C_2$ to $C_{18}$ alkoxyalkyl; substituted or unsubstituted $C_3$ to $C_{18}$ cyclic acetals; substituted or unsubstituted $C_7$ to $C_{18}$ carboaryloxy; linear, branched, and cyclic $C_2$ to $C_{18}$ carboalkoxy; substituted or unsubstituted $C_7$ to $C_{18}$ arylcarbonyl; and substituted or unsubstituted $C_2$ to $C_{18}$ alkylcarbonyl.

**[0049]** In the first step of the generalized reaction scheme shown in Scheme I, the phosphorochloridite (Structure II) reacts with a bisaryl compound HO-Q-OH (having Structure III, IV, or V) to give a monophosphite intermediate (Structure X). A suitable tertiary organic amine, including a basic nitrogen atom or a plurality of nitrogen atoms, such as a triorganoamine or a tertiary aromatic amine, can be present to neutralize the acid (HCl) formed from the reaction of the phosphorochloridite with the bisaryl compound. The monophosphite intermediate (Structure X) can then either react intermolecularly with phosphorochloridite to give the desired DLS (Structure I), or it can react intramolecularly to produce the cyclic triorganophosphite co-product of Structures VI, VII, and VIII, which are referred to herein as C-phite ligand structure, or CLS.

**[0050]** The intramolecular reaction of the monophosphite intermediate (Structure X) produces one equivalent each of the cyclophosphite and aryl alcohol, $R^1$-OH or $R^2$-OH, that originates from the phosphorochloridite. In some examples, aryl alcohol $R^1$-OH or $R^2$-OH can also be produced by other routes, as described herein. Depending on the concentration of phosphorochloridite, the aryl alcohol can react with another equivalent of the phosphorochloridite to give the acyclic triorganophosphite co-product of Structure IX, which is referred to herein as T-phite ligand structure, or TLS. This intramolecular reaction of the monophosphite intermediate thus can cause both the bisaryl compound and the phosphorochloridite to be converted to undesired product, causing lower selectivity for DLS production as a result of TLS and CLS production. In some examples, a greater amount of steric bulk in the bisaryl compound, in the phosphorochloridite, or in both the bisaryl compound and the phosphorochloridite can result in a greater proportion of TLS and CLS production and lower selectivity for DLS production.

**[0051]** Phosphorochloridites can be synthesized by stepwise reaction of $PCl_3$ with aryl alcohols, $R^1OH$ and $R^2OH$, in the presence of a suitable organic base to first prepare a phosphorodichloridite, for example $(R^1O)PCl_2$, followed by further reaction to prepare the phosphorochloridite, for example $(R^1O)(R^2O)PCl$, illustrated herein as Structure II. Syntheses for phosphorochloridites of Structure II are disclosed, for example, in PCT Publication WO 2004/050588.

**[0052]** Scheme II shows a generalized reaction scheme for hydrolysis of the phosphorochloridite. The phosphorochloridite can react with water to generate ligand hydrolysis products (LHPs), which can include acidic phosphorus-containing compounds (Structures XI and XII), phosphorous acid ($H_3PO_3$) or other phosphorus-containing acids, and aryl alcohol originating from the phosphorochloridite ($R^1OH$ or $R^2OH$). The phosphorochloridite can also react with the initial hydrolysis product (Structure XI) to form a phosphorus-containing acid anhydride (Structure XI).

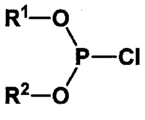


Scheme II

**[0053]** Empirically, as phosphorochloridite conversion increases, the intramolecular reaction rate for conversion of the monophosphite intermediate (Structure X) to CLS (Structures VI, VII, or VIII) and then to TLS (Structure IX) increases and selectivity to the desired DLS (Structure I) decreases. At high phosphorochloridite concentration, the rate for conversion of the monophosphite intermediate to DLS is increased compared to that in more dilute reaction conditions. Furthermore, dilute solutions can offer additional opportunity for reaction of the phosphorochloridite with any water contamination present to allow subsequent formation of acidic phosphorus-containing compounds, which can act as catalysts for the undesired intramolecular reaction to form CLS. Limiting the concentration of the monophosphite intermediate (Structure X) in the reaction mixture can help to achieve maximum selectivity for formation of DLS. Limiting the concentration of the monophosphite intermediate in the reaction mixture can limit the formation of undesired co-products such as TLS or CLS.

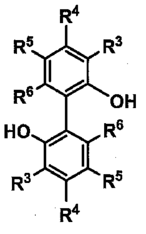
Contacting

**[0054]** Various embodiments of the present invention include contacting a phosphorochloridite of Structure II,

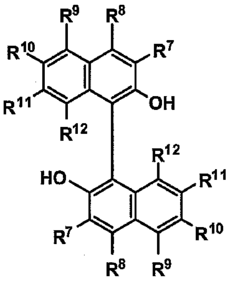


Structure II

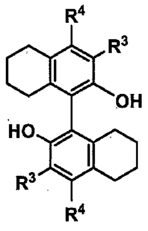
with an X-OH compound (e.g. a bisaryl compound) selected from the group consisting of Structure III, Structure IV, and Structure V,



Structure III



Structure IV



Structure V

and a tertiary organic amine to provide a reaction mixture including a DLS of Structure I. The contacting includes adding the bisaryl compound to the phosphorochloridite in a first serial addition, to provide the first reaction mixture. The contacting also includes adding the second serial addition, including at least one of the bisaryl compound, water, or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the second reaction mixture. The contacting can either include adding a third addition or the second reaction mixture is the final reaction mixture. The third addition, if performed, can include adding a compound selected from the group consisting of the bisaryl compound, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture.

**[0055]** The contacting can be any suitable contacting. In one example, the contacting can include adding any suitable material or mixture of suitable materials to any other suitable material or mixture or suitable materials, and can occur in a continuous or a batch fashion. The addition of one or more compounds to one or more other compounds can take place over any suitable period of time; one of skill in the art will readily recognize the value of controlling addition rate in chemical reactions, particularly in large scale chemical reactions. In one example, contacting can include feeding the bisaryl compound to a mixture of phosphorochloridite and tertiary organic amine. In another example, contacting can include feeding the X-OH compound (e.g. the bisaryl compound) and the tertiary organic amine separately to the phosphorochloridite. In another example, contacting can include feeding the X-OH compound (e.g. the bisaryl compound) and the tertiary organic amine as a mixture to the phosphorochloridite. For example, contacting can include feeding the X-OH compound (e.g. the bisaryl compound) continuously or discontinuously to a stirred vessel including the phosphorochloridite and tertiary organic amine. In another example, contacting can include feeding the X-OH compound (e.g. the bisaryl compound) continuously or discontinuously to a tubular reactor including continuous flow of a mixture of the phosphorochloridite and tertiary organic amine.

**[0056]** As described further below, the first serial addition includes addition of the X-OH and other materials. For example, the first serial addition can include addition of bisaryl compound or a mixture of bisaryl compound and other materials. As described further below, the second or third serial addition can also include addition of bisaryl compound or a mixture of bisaryl compound and other materials. However, in some embodiments, the second or third serial addition does not include bisaryl compound.

**[0057]** In some embodiments, the contacting can occur in a well-mixed reaction zone. Suitable mixing methods include those appropriate to the size and shape of the reaction vessel. Non-limiting examples of mixing methods include suitable methods known to those skilled in the art such as mechanical stirrerers, static mixers, nozzles, perforated pipes and downcomer trays. In some examples, liquids can be added using liquid distributors such as nozzles, perforated pipes, and downcomer trays. In some examples, flowing a liquid (e.g. bisaryl solution and tertiary organic amine) through at least one feed line that directs the liquid toward an impeller located below the upper liquid surface can help ensure efficient mixing of the liquid with the phosphorochloridite in a turbulent mixing zone of the reaction mixture. In some embodiments, poor mixing of the bisaryl compound or bisaryl solution with the phosphorochloridite can result in localized high concentrations of both bisaryl compound and monophosphite intermediate of Structure X, which can result in poorer selectivities for DLS formation.

**[0058]** In some examples, the method can produce phosphorus-containing ligand in the final reaction mixture with a molar selectivity from the phosphorochloridite compound such that the total molar percentage of phosphorus in the final reaction mixture as phosphorus-containing ligand (e.g. DLS) is between about 55% and about 65%, or between about 65% and about 75%, or between about 75% and about 85%, or between about 85% and about 90%, or between about 90% and about 95%, or between about 95% and about 100%.

**[0059]** In some embodiments, the method can include controlling the feeding such that a phosphorochloridite concentration is greater than or equal to an average distribution of about 0.02 moles per liter in the reaction mixture during the stage of the contacting, for example wherein phosphorochloridite conversion is from about 0% to about 90%. In some embodiments, the phosphorochloridite concentration is between an average distribution of about 0.02 and about 2.0 moles per liter in the reaction mixture during the stage of the contacting, for example wherein phosphorochloridite conversion is from about 0% to about 90%.

**[0060]** In various aspects, the method can include feeding the bisaryl compound to the phosphorochloridite at a feed rate between about 0.04 and about 10 molar equivalents per hour, relative to total moles of phosphorochloridite undergoing the contacting by the method. For example, feeding the bisaryl compound to the phosphorochloridite at a feed rate between about 0.5 and about 10 molar equivalents per hour.

**[0061]** In some examples, the first reaction mixture has a stoichiometric excess of phosphorochloridite. In some examples, the second reaction mixture has a stoichiometric excess of phosphorochloridite.

**[0062]** In some embodiments water can be detrimental to the selectivity of DLS formation. In some examples, water can be introduced to the reaction mixture via any feed stream, for example with the bisaryl compound, the tertiary organic amine, or a combination of the bisaryl compound and the tertiary organic amine. In examples, prior to the contacting with the phosphorochloridite, water can be at least partially separated from the bisaryl compound and the tertiary organic amine by phase separation, distillation, azeotropic distillation, contact with dried molecular sieves, drying columns, and other suitable methods known in the art.

**[0063]** In one embodiment of the present invention, the first serial addition can include the X-OH compound (e.g. the bisaryl compound) in sufficient quantity such that the conversion of the phosphorochloridite is about 85% to about 95% in the first reaction mixture; the second serial addition can include a smaller amount of the X-OH compound than the amount of the X-OH compound added in the first serial addition.

**[0064]** In another embodiment of the present invention, the first serial addition can include the X-OH compound in sufficient quantity such that the conversion of the phosphorochloridite is about 85% to about 91% in the first reaction mixture; the second serial addition can include an alcohol having the chemical structure $R^1$-OH or $R^2$-OH in sufficient quantity such that remaining phosphorochloridite is converted to a suitable side-product (e.g. the TLS) in the second (e.g. final) reaction mixture. In some examples, the second serial addition can include an alcohol having the chemical structure $R^1$-OH or $R^2$-OH in sufficient quantity such that in the second reaction mixture phosphorochloridite conversion is about 100%.

**[0065]** The first, second, and final reaction mixture can have a composition that evolves over time, as the reactants are gradually converted into products and an approximate equilibrium state is achieved in which the reaction products reach a relatively steady concentration, as will be readily understood by one of skill in the art. The amount of time to reach the approximately equilibrium state can be, for example, about 1 second to about 10 days, about 1 minute to about 5 days, or about 10 minutes to about 1 day, or about 1 hour to about 10 hours. In another example, the time to reach the approximately equilibrium state can be, for example, about 1 second to about 1 minute, or about 1 minute to about 1 hour, about 1 hour to about 5 hours, or about 5 hours to about 24 hours. Generally, when the composition of the first, second, or final reaction mixture is referred to herein, unless otherwise indicated, reference is being made to the composition of the first reaction mixture after the particular addition step that gives rise to the reaction mixture has completed (e.g. the first addition, the second addition, or the third addition if performed), the reaction has essentially gone to completion, and an approximately equilibrium state has been achieved.

**[0066]** The contacting also includes determining a mole percent of phosphorus present in the first reaction mixture as at least one side-product. The contacting also includes using a comparison of the mole percent of phosphorus present in the first reaction mixture as the at least one side-product to a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and an alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a second serial addition. The at least one side-product in such determination can be, for example, CLS, TLS, LHP, phosphorochloridite, any suitable side-product, or any combination thereof.

Hydrocarbon Solvent

**[0067]** In some embodiments, the reaction mixture can include at least one aromatic hydrocarbon solvent. The hydrocarbon solvent can include any suitable hydrocarbon solvent. The aromatic hydrocarbon solvent can be selected from the group consisting of $C_6$ to $C_{18}$ aromatic hydrocarbons. In some embodiments, the method can include feeding the X-OH compound to the phosphorochloridite as a solution of the X-OH compound including the X-OH compound and a hydrocarbon solvent. In some examples, the hydrocarbon solvent can be hydrocarbons selected from the group consisting of linear acyclic $C_5$ to $C_{18}$ aliphatic, branched acyclic $C_5$ to $C_{18}$ aliphatic, unsubstituted cyclic $C_5$ to $C_{18}$ aliphatic, substituted cyclic $C_5$ to $C_{18}$ aliphatic, unsubstituted $C_6$ to $C_{10}$ aromatic, and $C_6$ to $C_{18}$ substituted aromatic hydrocarbons. The hydrocarbon solvent can be selected from the group consisting of hydrocarbons whose boiling point is between 70 °C and 145 °C at atmospheric pressure. Examples of suitable aromatic hydrocarbon solvents include $C_{1-5}$-substituted benzenes, $C_{1-5}$-substituted phenol, and xylenes or xylenols of any suitable substitution pattern. Specific examples of suitable aromatic hydrocarbon solvents include toluene. In some examples, the X-OH compound is fed to the phosphorochloridite as a solution include the X-OH compound and hydrocarbon solvent.

Temperature of Contacting

**[0068]** The temperature of contacting can be any suitable temperature. In some embodiments, the contacting can occur at a temperature within a temperature range listed in the left-hand column of Table 1. In other embodiments, the contacting of the method can occur at a temperature within a temperature range listed in the right-hand column of Table 1. In other aspects of the invention, the reaction mixture includes a hydrocarbon solvent and the boiling point of the reaction mixture at one atmosphere (1 atm) in the right-hand column of Table 1 is approximately equal to the boiling point of the hydrocarbon solvent. In various embodiments, a hydrocarbon solvent can be introduced into the reaction mixture with the phosphorochloridite, the X-OH compound (e.g. the bisaryl compound), tertiary organic amine, with any combination of such members, or independent of these reactants.

**[0069]** Table 1. Suitable Temperature Ranges for a Contacting Step, in Various Embodiments

| Temperature Range | Temperature Range |
|---|---|
| about 10 to about 110°C | about 10°C to the boiling point of the mixture at 1 atm |
| about 15 to about 110°C | about 15°C to the boiling point of the mixture at 1 atm |
| about 20 to about 110°C | about 20°C to the boiling point of the mixture at 1 atm |
| about 25 to about 110°C | about 25°C to the boiling point of the mixture at 1 atm |
| about 30 to about 110°C | about 30°C to the boiling point of the mixture at 1 atm |
| about 35 to about 110°C | about 35°C to the boiling point of the mixture at 1 atm |
| about 40 to about 110°C | about 40°C to the boiling point of the mixture at 1 atm |
| about 45 to about 110°C | about 45°C to the boiling point of the mixture at 1 atm |
| about 50 to about 110°C | about 50°C to the boiling point of the mixture at 1 atm |
| about 55 to about 110°C | about 55°C to the boiling point of the mixture at 1 atm |
| about 60 to about 110°C | about 60°C to the boiling point of the mixture at 1 atm |

Tertiary Organic Amine

**[0070]** The tertiary organic amine can be any suitable tertiary organic amine, and can be added in any suitable amount. In some embodiments, tertiary organic amine can be added in quantity sufficient to neutralize the HCl co-product in the reaction mixture. The amine can accelerate reaction rates and can limit acid-catalyzed chemistries that can reduce selectivities of DLS formation. In some examples, the method includes precipitating a tertiary organic amine hydrogen chloride salt from the reaction mixture during the contacting step. In some examples, both the selection of the tertiary organic amine and the contacting in the presence of a hydrocarbon solvent can precipitate a tertiary organic amine hydrogen chloride salt from the reaction mixture.

**[0071]** Examples of suitable tertiary organic amines including a single basic nitrogen atom can be a (R')(R'')(R''')N compound wherein R', R'', and R''' are independently selected from the group consisting of $C_1$ to $C_{10}$ alkyl and $C_6$ to $C_{10}$ aryl radicals, can be a tertiary aromatic amine compound, for example pyridine, or can be combinations of tertiary organic amines including a single basic nitrogen atom. One example of a suitable amine includes a trialkylamine with the alkyl group individually selected and having 1 to 10 carbon atoms, such as triethylamine. Other examples include tertiary organic amines including a plurality of basic nitrogen atoms have nitrogen atoms with no N-H bonds; for example N,N,N',N'-tetramethylethylenediamine. In some examples, the first addition, the second addition, the third addition (if performed), or any combination thereof can be carried out in the presence of a stoichiometric excess of the tertiary organic amine.

Weight Percent Ranges of Components

**[0072]** Other examples of molar ranges of various reactants are given herein, the ranges given in this section are non-limiting examples.

**[0073]** In some examples, the phosphorochloridite can be from about 10 wt% to about 90 wt%, about 20 wt% to about 80 wt%, or about 30 wt% to about 70 wt% of the total amount of phosphorochloridite, bisaryl compound, and tertiary organic amine added in all of the first, second, and third addition (if performed). In some embodiments, the phosphorochloridite can be from about 40 wt% to about 60 wt%, about 45 wt% to about 55 wt%, or about 48 wt% to about 52 wt% of the total amount of phosphorochloridite, bisaryl compound, and tertiary organic amine added.

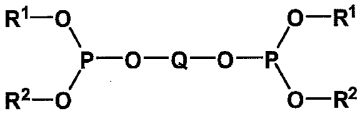
**[0074]** In some examples, the bisaryl compound can from about 1 wt% to about 80 wt%, about 5 wt% to about 70 wt%, or about 10 wt% to about 60 wt% of the total amount of phosphorochloridite, bisaryl compound, and tertiary organic amine added in all of the first, second, and third addition (if performed). In some embodiments, the bisaryl compound can from about 10 wt% to about 45 wt%, about 20 wt% to about 35 wt%, or about 25 wt% to about 30 wt% of the total amount of phosphorochloridite, bisaryl compound, and tertiary organic amine added.

**[0075]** In some examples, the tertiary organic amine can be from about 1 wt% to about 99 wt%, about 5 wt% to about 70 wt%, or about 10 wt% to about 60 wt% of the total amount of phosphorochloridite, bisaryl compound, and tertiary organic amine added in all of the first, second, and third addition (if performed). In some embodiments, the tertiary organic amine can be from about 5 wt% to about 40 wt%, about 15 wt% to about 30 wt%, or about 20 wt% to about 25 wt% of the total amount of phosphorochloridite, bisaryl compound, and tertiary organic amine added.

**[0076]** In some examples, the aromatic hydrocarbon solvent can be present in from about 1 wt% to about 99.999 wt%, about 5 wt% to about 80 wt%, or about 10 wt% to about 60 wt% of the total amount of aromatic hydrocarbon solvent, phosphorochloridite, bisaryl compound, and tertiary organic amine added in all of the first, second, and third addition (if performed). In some embodiments, the aromatic hydrocarbon solvent can be present in from about 5 wt% to about 70 wt%, about 15 wt% to about 50 wt%, or about 25 wt% to about 40 wt% of the total amount of aromatic hydrocarbon solvent, phosphorochloridite, bisaryl compound, and tertiary organic amine added.

D-phite Ligand Structure (DLS)

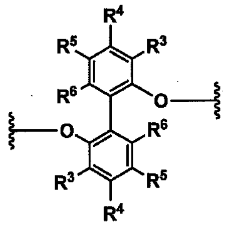
**[0077]** As described above, in a specific embodiment the method of the present invention can produce a diphosphite ligand structure (DLS) having the chemical structure of Structure I,

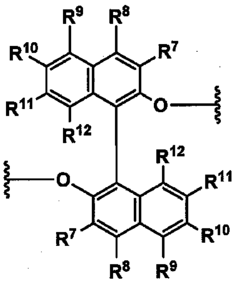


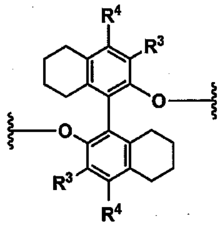
**Structure I.**

**[0078]** In Structure I, $R^1$ and $R^2$ can be the same or different, substituted or unsubstituted, monovalent aryl groups. In some examples, $R^1$ and $R^2$ can be substituted or unsubstituted aryl groups. In some examples, $R^1$ and $R^2$ can be $C_{1-10}$ alkyl-substituted phenyl groups. In some examples, $R^1$ and $R^2$ can be the same. In some examples, $R^1$ and $R^2$ can be xylenyl groups (e.g. monovalent xylene groups), for example 2,4-xylenyl groups.

**[0079]** In Structure I, O-Q-O is a divalent species of the bisaryl compound having Structures III, IV, and V. Thus, O-Q-O can be represented by one of the following three structures:

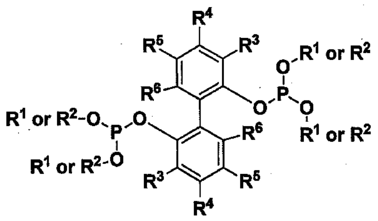






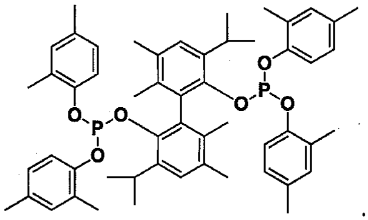
wherein each of $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ can be any suitable functional group. In one example, $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ are independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups. In one example, $R^3$ to $R^{12}$ can be linear, branched, and cyclic $C_1$ to $C_{18}$ alkyl; substituted or unsubstituted $C_6$ to $C_{18}$ aryl; substituted or unsubstituted $C_6$ to $C_{18}$ aryloxy; linear, branched, and cyclic $C_1$ to $C_{18}$ alkyloxy; linear and branched $C_2$ to $C_{18}$ alkoxyalkyl; substituted or unsubstituted $C_3$ to $C_{18}$ cyclic acetals; substituted or unsubstituted $C_7$ to $C_{18}$ carboaryloxy; linear, branched, and cyclic $C_2$ to $C_{18}$ carboalkoxy; substituted or unsubstituted $C_7$ to $C_{18}$ arylcarbonyl; and substituted or unsubstituted $C_2$ to $C_{18}$ alkylcarbonyl.

**[0080]** In some embodiments, DLS can be represented by the following structure:



wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

**[0081]** In some embodiments, DLS can be represented by the following structure:



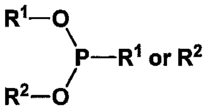
Thus, $R^1$ and $R^2$ can be 2,4-xylenyl, $R^3$ can be isopropyl, $R^4$ can be hydrogen, and $R^5$ and $R^6$ can be methyl. In some embodiments, DLS compounds such as the compound described in this paragraph can be identified in $^{31}P$ NMR spectra by peaks occurring at about 131.8 ppm.

**[0082]** In some embodiments, in the final reaction mixture, the percentage of phosphorus present as the phosphorus-containing ligand structure can be from about 1% to about 100% or about 30% to about 100%, or about 50% to about 99%, or about 55% to about 95%, or about 60% to about 90%, or about 60% to about 80%, or about 62% to about 85%, or about 64% to about 80%, or about 65%, or about 70%.

**[0083]** In some embodiments, in the final reaction mixture, the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 65%, and the percentage of phosphorus present as the LHP is less than no more than about 5%. In some embodiments, in the final reaction mixture, the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 70%, and the percentage of phosphorus present as the LHP is less than no more than about 3.5%. In some embodiments, in the final reaction mixture, the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 65%, and the percentage of phosphorus present as the CLS is less than about 5%. In some embodiments, in the final reaction mixture, the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 70%, and the percentage of phosphorus present as the CLS is less than about 3.5%.

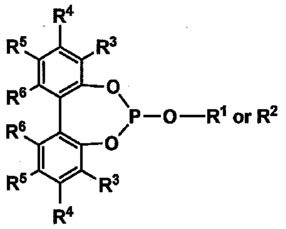
### T-phite Ligand Structure (TLS) and C-phite Ligand Structure (CLS)

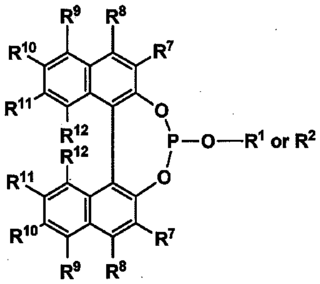
**[0084]** As described above in Scheme I, in some embodiments, the method can produce at least one phosphorus-containing co-product in the final reaction mixture selected from the group consisting of $P(OR^1)(OR^2)_2$, $P(OR^1)_2(OR^2)$, $P(OR^1)_3$ (when $R^2$=$R^1$), $P(OR^2)_3$ (when $R^1$=$R^2$), TLS structures shown below as Structure IX:



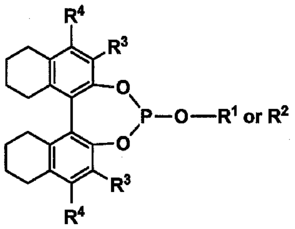
**Structure IX,**

and a compound of CLS Structures VI, VII, or VIII, shown below:





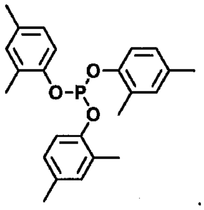
**Structure VI** **Structure VII**



**Structure VIII.**

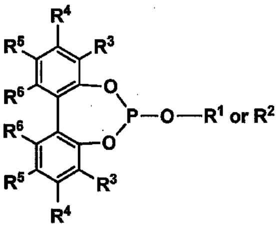
**[0085]** In the TLS and CLS structures given above, $R^1$ and $R^2$ can be the same or different, substituted or unsubstituted, monovalent aryl groups. In some examples, $R^1$ and $R^2$ can be substituted or unsubstituted aryl groups. In some examples, $R^1$ and $R^2$ can be $C_{1-10}$ alkyl-substituted phenyl groups. In some examples, $R^1$ and $R^2$ can be the same. In some examples, $R^1$ and $R^2$ can be xylenyl groups (e.g. monovalent xylene groups), for example 2,4-xylenyl groups. Each of $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ can be any suitable functional group. In one example, $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ are independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups. In one example, $R^3$ to $R^{12}$ can be linear, branched, and cyclic $C_1$ to $C_{18}$ alkyl; substituted or unsubstituted $C_6$ to $C_{18}$ aryl; substituted or unsubstituted $C_6$ to $C_{18}$ aryloxy; linear, branched, and cyclic $C_1$ to $C_{18}$ alkyloxy; linear and branched $C_2$ to $C_{18}$ alkoxyalkyl; substituted or unsubstituted $C_3$ to $C_{18}$ cyclic acetals; substituted or unsubstituted $C_7$ to $C_{18}$ carboaryloxy; linear, branched, and cyclic $C_2$ to $C_{18}$ carboalkoxy; substituted or unsubstituted $C_7$ to $C_{18}$ arylcarbonyl; and substituted or unsubstituted $C_2$ to $C_{18}$ alkylcarbonyl.

**[0086]** In some embodiments, TLS can be represented by the following structure:



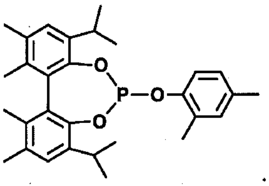
Thus, $R^1$ or $R^2$ can be 2,4-xylenyl. In some embodiments, TLS compounds, such as the compound described in this paragraph, can be identified in $^{31}P$ NMR spectra by peaks occurring at about 131.2 ppm.

**[0087]** In some embodiments, CLS can be represented by the following structure:



wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1\text{-}10}$ alkyl.

**[0088]** In some embodiments, CLS can be represented by the following structure:



Thus, $R^1$ or $R^2$ can be 2,4-xylenyl, $R^3$ can be isopropyl, $R^4$ can be hydrogen, and $R^5$ and $R^6$ can be methyl. In some embodiments, CLS compounds such as the compound described in this paragraph can be identified in $^{31}$P NMR spectra by peaks occurring at about 136.0 ppm.

Pre-Determined Limits

**[0089]** In various examples, the contacting includes providing pre-determined limits for the percent of phosphorus present as particular products in a reaction mixture, for example as particular side products in the final reaction mixture. The pre-determined limit can be any suitable pre-determined limit. The pre-determined limits can be provided at any suitable time, such as for example prior to the first addition, prior to the second addition, or prior to the third addition (if performed). In one example, the percent of phosphorus present as particular products in a reaction mixture is a molar percent. In another example, the percent of phosphorus present as particular products in a reaction mixture can be based on mass or based on any other suitable measure. The pre-determined limit can be based on all phosphorus-containing compounds in the reaction mixture. In one example, the pre-determined limit can be the desired specification limit for the percent of phosphorus present as the particular product in the final reaction mixture. In another example, the pre-determined limit can be some value below the desired specification limit for the percent of phosphorus present as the particular product in the final reaction mixture. By choosing a pre-determined limit lower than the specification limit, this can help to ensure that the actual specification limit is achieved in the final product mixture, and can allow for a margin of error. However, in some embodiments, no margin of error is used, and the pre-determined limit corresponds to the desired specification limit for the percent of phosphorus present as the particular product in the final reaction mixture.

**[0090]** In some examples, the contacting includes providing a pre-determined limit for the mole percent of phosphorus present as CLS in the final reaction mixture. The pre-determined limit for the mole percent of phosphorus present as CLS in the final reaction mixture can be any suitable pre-determined limit. In one example, the pre-determined limit for the mole percent of phosphorus present as CLS in the final reaction mixture is about 0 mol% to about 99 mol%, about 0 mol% to about 50 mol%, or about 0 mol% to about 5 mol%. In another example, the pre-determined limit for the mole percent of phosphorus present as CLS in the final reaction mixture is about 0 mol% to about 16 mol%, about 1 mol% to about 8 mol%, or about 2 mol% to about 4 mol%. In another example, the pre-determined limit for the mole percent of phosphorus present as CLS in the final reaction mixture is about 0 mol% to about 6 mol%, about 0 mol% to about 4 mol%, or about 0 mol% to about 2 mol%. Any pre-determined limit given in this paragraph can also be an example of the percentage of phosphorus present as the CLS in the final reaction mixture.

**[0091]** In some examples, the contacting includes providing a pre-determined limit for the mole percent of phosphorus present as TLS in the final reaction mixture. The pre-determined limit for the mole percent of phosphorus present as TLS in the final reaction mixture can be any suitable pre-determined limit. In one example, the pre-determined limit for the mole percent of phosphorus present as TLS in the final reaction mixture is about 0 mol% to about 100 mol%, or about 0 mol% to about 50 mol%. In another example, the pre-determined limit for the mole percent of phosphorus present as TLS in the final reaction mixture is about 2 mol% to about 50 mol%, about 5 mol% to about 40 mol%, or about 10 mol% to about 30 mol%. In another example, the pre-determined limit for the mole percent of phosphorus present as TLS in the final reaction mixture is about 3 mol% to about 80 mol%, about 7 mol% to about 40 mol%, or about 14 mol% to about 21 mol%. Any pre-determined limit given in this paragraph can also be an example of the percentage of phosphorus present as the TLS in the final reaction mixture.

**[0092]** In one example, the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture is about 0 mol% to about 99 mol%, about 0 mol% to about 50 mol%, or about 0 mol% to about 5 mol%. The pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture can be any suitable pre-determined limit. In another example, the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture is about 0 mol% to about 16 mol%, about 1 mol% to about 8 mol%, or about 2 mol% to about 4 mol%. In another example, the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture is about 0 mol% to about 6 mol%, about 0 mol% to about 4 mol%, or about 0 mol% to about 2 mol%. Any pre-determined limit given in this paragraph can also be an example of the percentage of phosphorus present as the LHP in the final reaction mixture.

**[0093]** Providing a pre-determined limit can include providing a pre-determined limit for the percent phosphorus in the final reaction mixture that is present as one or more of TLS, CLS, LHP, DLS, any other suitable side-product.

Percent Conversion

**[0094]** In some embodiments, decisions about the composition of the first serial addition can be made including using a pre-determined goal for conversion of the phosphorochloridite in the first reaction mixture. Thus, contacting can include providing a pre-determined goal for the conversion of the phosphorochloridite in the first reaction mixture. The pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture can be provided before the first addition is added. Contacting can also include using the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture to determine the amount of bisaryl compound to add in the first serial addition. For example, the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture can be used to determine the amount of bisaryl compound to add in the first serial addition such that the percent conversion of the phosphorochloridite in the first reaction mixture is at or above the pre-determined goal.

**[0095]** The pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture can be any suitable pre-determined goal. In some embodiments, the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture is about 30% to about 100%, or about 70% to about 100%, or about 80% to about 97%, or about 85% to about 95%, or about 88% to about 92%, or about 90%.

**[0096]** In some embodiments, decisions about the composition of the second serial addition can be made including using a pre-determined goal for conversion of phosphorochloridite in the second reaction mixture. Thus, contacting can include providing a pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture. In some embodiments, the providing of the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture can occur before the first serial addition is added. In other embodiments, the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture can be provided after the first serial addition is added. Contacting can also include, after adding the first serial addition, determining the percent conversion of the phosphorochloridite in the first reaction mixture. Contacting can also include, before adding the second serial addition, using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of a particular compound to add in the second serial addition. For example, contacting can include using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture to determine the amount of a compound selected from the group consisting of the X-OH, water, or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH to add in the second serial addition such that the percent conversion of the phosphorochloridite in the second reaction mixture is at or above the pre-determined goal.

**[0097]** The pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture can be any suitable pre-determined goal. In some embodiments, the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture is about 50% to about 100%, or about 70% to about 100%, or about 90% to about 99%, or about 95% to about 99%, or about 98%.

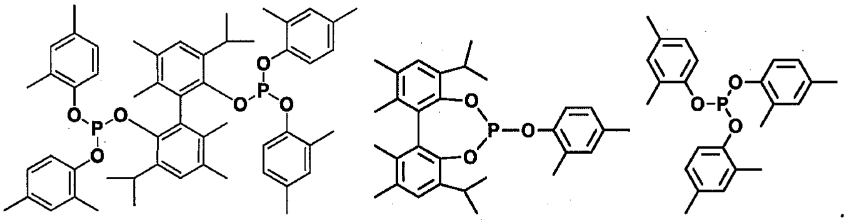
**[0098]** In some embodiments, the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture is about 80% to about 100%. In some examples, the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture is about 96% to about 99%. In some examples, the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture is about 85% to about 95%. In some examples, the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture is about 90%.

### Ligand Hydrolysis Product (LHP)

**[0099]** In some embodiments, decisions about the composition of the second serial addition can be made including using a pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture.

**[00100]** In some embodiments, the ligand hydrolysis products can be any suitable hydrolysis product of any material present in the reaction mixture. When LHPs are discussed herein, any suitable number of LHPs can be referred to, including some or all LHPs. An LHP can include a product derived by a process including hydrolysis of the phosphorus-containing ligand or of the phosphorochloridite. An LHP can include a product derived by a process including hydrolysis of a product derived from the phosphorus-containing ligand or from the phosphorochloridite. An LHP can include a product derived by a process including reaction of a hydrolysis product of the phosphorus-containing ligand or of the phosphorochloridite, or reaction of the hydrolysis product of the a product derived from the phosphorus-containing ligand or from the phosphorochloridite. The LHPs can include any hydrolyzed product of a DLS, TLS, CLS, or the phosphorochloridite, wherein any one P-OR bond therein and any number of P-OR bonds therein is replaced with a P-OH bond. The LHPs can also include materials derived from ligand hydrolysis products, such as for example anhydrides, formed by, for example, reaction of two P-OR bonds to form a P-O-P structure.

**[00101]** In some embodiments, LHP compounds can be derived from the structures shown below:



In some embodiments, LHP compounds such as those described in the present paragraph can be identified using $^{31}P$ NMR by peaks occurring at about 30 ppm to about -20 ppm.

Determining Mole Percentages and Conversion

**[00102]** The contacting can include determining the mole percent of phosphorus present in the first or second reaction mixture as a side-product. For example, the contacting can include determining the mole percent of phosphorus present in the first or second reaction mixture of CLS, TLS, LHP, or any other suitable side-product. In some embodiments, determining the mole percent of phosphorus present in the first or second reaction mixture as one or more particular side products can include withdrawing samples to analyze the liquid reaction mixture, for example by $^{31}P$ NMR, $^{1}H$ NMR, liquid or gas chromatography, mass spectrometry, infrared or UV spectroscopy, or any combination thereof. The samples withdrawn can be any suitable size, and the analytical method used can be any suitable analytical method.

**[00103]** For example, using NMR analysis techniques well known in the art, the integration of NMR peaks that correspond to particular compounds can be used to calculate the mole ratio of various compounds in a reaction mixture, for example based on proportionality between integration ratios and molar ratios. Based a knowledge of the total amounts of reagents added and/or already present in the mixture prior to the last addition, the molar ratios can be used to determine the molar percent of phosphorus present as particular products in the reaction mixture.

First Serial Addition

**[00104]** The contacting includes adding the X-OH compound to the phosphorochloridite in a first serial addition, to provide the first reaction mixture. Any suitable quantity of the X-OH compound can be added to any suitable quantity of the phosphorochloridite in the first serial addition, and the addition can take place at any suitable rate. The first serial addition can occur at any suitable temperature. In one example, the X-OH compound can be a bisaryl compound.

**[00105]** In some examples, the contacting can include using a pre-determined limit for the mole percent of phosphorus present as at least one side-product in the final reaction mixture to determine an amount of the X-OH to add in the first serial addition to cause the mole percent of phosphorus present in the first reaction mixture as the at least one side-product to be less than the pre-determined limit of the mole percent of phosphorus present as the at least one side-product in the final reaction mixture.

**[00106]** In some embodiments, the amount of the X-OH added in the second serial addition can be less than the amount of the X-OH added in the first serial addition.

**[00107]** In some examples, the contacting includes providing a pre-determined goal for a conversion of phosphorochloridite in the first reaction mixture. The contacting can further include, before adding the first serial addition, using the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture to determine the amount of the X-OH to add in the first serial addition, such that the conversion of phosphorochloridite in the first reaction mixture is at or above the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture.

**[00108]** In various embodiments, the first reaction mixture can have a stoichiometric excess of phosphorochloridite.

Second Serial Addition

**[00109]** The contacting also includes adding the second serial addition to the second reaction mixture, including at least one of the X-OH compound, water, or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the second reaction mixture. Any suitable quantity of at least one of the X-OH compound, water, or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH can be added to the first reaction mixture in the second serial addition, and the addition can take place at any suitable rate. The second serial addition can occur at any suitable temperature. In one example, the X-OH compound can be a bisaryl compound. In embodiments in which third addition steps are not performed, the second reaction mixture is the final reaction mixture. In embodiments in which third addition steps are performed, the second reaction mixture is not the final reaction mixture.

**[00110]** In some embodiments, the contacting can include using a pre-determined limit for the mole percent of phosphorus present as at least one side-product in the final reaction mixture to determine an amount of the X-OH to add in the first or second serial addition to cause a mole percent of phosphorus present in the second reaction mixture as the at least one side-product to be less than the pre-determined limit of the mole percent of phosphorus present as the at least one side-product in the final reaction mixture.

**[00111]** In some examples, the amount of the X-OH added in the second serial addition is none.

**[00112]** In some embodiments, if the amount of the X-OH added in the second serial addition is none, then the second serial addition includes at least one of water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00113]** In some embodiments, using a comparison of the mole percent of phosphorus present in the first reaction mixture as the CLS to the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture to determine the amount of a compound to add in the second serial addition includes adding an amount of a compound in the second addition selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH sufficient to cause the mole percent of phosphorus in the second reaction mixture present as the CLS to be equal to or below the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture. In some examples, if the mole percent of phosphorus present in the first reaction mixture as the CLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, then the second serial addition includes water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH. In some examples, if the mole percent of phosphorus present in the first reaction mixture as the CLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, then the second serial addition does not include the X-OH.

**[00114]** In some embodiments, using a comparison of the mole percent of phosphorus present in the first reaction mixture as the TLS to the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture to determine the amount of a compound to add in the second serial addition includes adding an amount of a compound in the second addition selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH sufficient to cause the mole percent of phosphorus in the second reaction mixture present as the TLS to be equal to or below the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture. In some examples, if the mole percent of phosphorus present in the first reaction mixture as the TLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the second serial addition includes water. In some examples, if the mole percent of phosphorus present in the first reaction mixture as TLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the second serial addition does not include the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00115]** In some embodiments, using a comparison of the mole percent of phosphorus present in the first reaction mixture as the LHP to the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture to determine the amount of a compound to add in the second serial addition includes adding an amount of a compound in the second addition selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH sufficient to cause the mole percent of phosphorus in the second reaction mixture present as the LHP to be equal to or below the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture. In some examples, if the mole percent of phosphorus present in the first reaction mixture as LHP is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture, then the second serial addition includes the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH. In some examples, if the mole percent of phosphorus present in the first reaction mixture as LHP is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture, then the second serial addition does not include water.

**[00116]** In some examples, if in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition includes water. In some examples, if in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition does not include the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00117]** In some examples, the contacting includes providing a pre-determined goal for a conversion of phosphorochloridite in the second reaction mixture. The contacting can further include, after adding the first serial addition, determining the percent conversion of the phosphorochloridite in the first reaction mixture. And, the contacting can further include, before adding the second serial addition, using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of the X-OH to add in the second serial addition.

**[00118]** In some embodiments, the contacting includes providing a pre-determined goal for a conversion of phosphorochloridite in the second reaction mixture. The contacting can further include, after adding the first serial addition, determining the percent conversion of the phosphorochloridite in the first reaction mixture. The contacting can further include, before adding the second serial addition, using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of the X-OH to add in the second serial addition. In some examples, if in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor as the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or as the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction mixture is less than the pre-determined goal for the conversion of phosphorochloridite in the final reaction mixture, then the amount of the X-OH to add in the second serial addition is sufficient to make the percent conversion of the phosphorochloridite in the second reaction mixture equal to or above the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture. In some examples, if in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor as the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or as the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction mixture is less than the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture, then the second serial addition does not include water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00119]** In some embodiments, contacting can include providing a pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture. Contacting can further include, after adding the first serial addition, determining the mole percent of phosphorus present as LHP in the first reaction mixture. The contacting can further include, before adding the second serial addition, using a comparison of the mole percent of phosphorus present as LHP in the first reaction mixture to the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture to determine the composition of the second serial addition. In some examples, if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition includes the alcohol having the chemical structure $R^1$-OH or $R^2$-OH. In some examples, if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition does not include the X-OH or water.

**[00120]** In some embodiments, the contacting can include providing a pre-determined goal for a conversion of phosphorochloridite in the second reaction mixture. The contacting can further include, after adding the first serial addition, determining the percent conversion of the phosphorochloridite in the first reaction mixture. If in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition includes water. If in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the second serial addition includes water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH. If in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor as the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction product is less than the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture, then the second serial includes a sufficient amount of the X-OH such that the percent conversion of the phosphorochloridite in the second reaction mixture is equal to or above the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture. In some examples, if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the second serial addition includes the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00121]** In some embodiments, contacting includes providing a pre-determined goal for a conversion of phosphorochloridite in the second reaction mixture. Contacting can further include, after adding the first serial addition, determining the percent conversion of the phosphorochloridite in the first reaction mixture and determining the mole percent of phosphorus present as LHP in the first reaction mixture. If in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition includes water. If in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition includes the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and if in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction product is less than the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture, then second serial addition includes X-OH in sufficient quantity such that the percent conversion of the phosphorochloridite in the second reaction mixture is equal to or above the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture. In some examples, if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is not equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition includes water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and if in the first reaction mixture the mole percent of phosphorus present as the TLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the CLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is not equal or to greater than the pre-determined limit for LHP content in the final reaction mixture, then the second addition includes water. In some examples, if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is not equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition does not include the X-OH; and, if in the first reaction mixture the mole percent of phosphorus present as the TLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the CLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is not equal or to greater than the pre-determined limit for LHP content in the final reaction mixture, then the second addition does not include water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00122]** In some embodiments, the weight ratio of the X-OH added in the first serial addition to the X-OH added in the second serial addition is from 9.0:1.0 to 9.9:1.0.

Optional Third Serial Addition

**[00123]** The contacting also either includes performing third addition steps, or the final reaction mixture is the second reaction mixture. If the contacting includes performing third addition steps, the final reaction mixture is not the second reaction mixture. If the contacting does not include performing third additional steps, the final reaction mixture is the second reaction mixture.

**[00124]** The third addition steps, if performed, include optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition. In some embodiments, if third addition steps are performed, the step of using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition, is performed. In other embodiments, if third addition steps are performed, the step of using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition is not performed. The third addition steps, if performed, include optionally determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product. In some embodiments, if the third addition steps are performed, the step of determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product is performed. In other embodiments, if the third addition steps are performed, the step of determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product is not performed. The third addition steps, if performed, include adding the third serial addition to the second reaction mixture, including a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture.

**[00125]** In some embodiments, the contacting includes using the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture to determine an amount of the X-OH to add in the third serial addition to cause a mole percent of phosphorus present in the final reaction mixture as the at least one side-product to be less than the pre-determined limit of the mole percent of phosphorus present as the at least one side-product in the final reaction mixture.

**[00126]** In some examples, the amount of the X-OH added in the third serial addition if performed is equal to or less than the amount of the X-OH added in the second serial addition. In some examples, the amount of the X-OH added in the third serial addition is none. In some examples, if the amount of the X-OH added in the third serial addition is none, then the third serial addition if performed includes at least one of water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00127]** In some embodiments, using a comparison of the mole percent of phosphorus present in the second reaction mixture as the CLS to the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture to determine the amount of a compound to add in the the third serial addition if performed includes adding an amount of a compound in the third addition selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH sufficient to cause the mole percent of phosphorus in the final reaction mixture present as the CLS to be equal to or below the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture. In some examples, if the mole percent of phosphorus present in the second reaction mixture as the CLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, then the third serial addition if performed includes water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH. In some examples, if the mole percent of phosphorus present in the second reaction mixture as the CLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, then the third addition if performed does not include the X-OH.

**[00128]** In some embodiments, using a comparison of the mole percent of phosphorus present in the second reaction mixture as the TLS to the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture to determine the amount of a compound to add in the third serial addition includes adding an amount of a compound in the third addition selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH sufficient to cause the mole percent of phosphorus in the final reaction mixture present as the TLS to be equal to or below the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture. In some examples, if the mole percent of phosphorus present in the second reaction mixture as the TLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the third serial addition if performed includes water. In some examples, if the mole percent of phosphorus present in the second reaction mixture as TLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the third serial addition if performed does not include the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00129]** In some embodiments, using a comparison of the mole percent of phosphorus present in the second reaction mixture as the TLS to the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture to determine the amount of a compound to add in the third serial addition includes adding an amount of a compound in the third addition selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH sufficient to cause the mole percent of phosphorus in the final reaction mixture present as the TLS to be equal to or below the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture. In some examples, if the mole percent of phosphorus present in the second reaction mixture as the TLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the third serial addition if performed includes water. In some examples, if the mole percent of phosphorus present in the second reaction mixture as TLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the third serial addition if performed does not include the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00130]** In some examples, if percent conversion of the phosphorochloridite in the second reaction mixture is less than about 100%, then the contacting further includes adding the third serial addition to the second reaction mixture, wherein the third serial addition includes a sufficient quantity of water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH such that following the third serial addition the phosphorochloridite conversion in the final reaction mixture is about 100%.

**[00131]** In some examples, contacting includes determining the percent conversion of the phosphorochloridite in the second reaction mixture and determining the mole percent of phosphorus present as TLS in the second reaction mixture, wherein if percent conversion of the phosphorochloridite in the second reaction mixture is less than about 100%, and if in the second reaction mixture the mole percent of phosphorus present as TLS is less than the pre-determined limit for the mole percent of phosphorus present as TLS in the final reaction mixture, then further including adding the third serial addition to the second reaction mixture, wherein the third serial addition includes a sufficient quantity of the alcohol having the chemical structure $R^1$-OH or $R^2$-OH such that following the third serial addition the conversion of the phosphorochloridite in the final reaction mixture is about 100%.

**[00132]** In some embodiments, if percent conversion of the phosphorochloridite in the second reaction mixture is less than about 100%, and if in the second reaction mixture the mole percent of phosphorus present as LHP is less than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the contacting further includes adding a third serial addition to the second reaction mixture, wherein the third serial addition includes a sufficient quantity of water such that following the third serial addition the conversion of the phosphorochloridite in the final reaction mixture is about 100%.

**[00133]** In some embodiments, the first serial addition includes the X-OH in sufficient quantity such that the conversion of the phosphorochloridite in the first reaction mixture is about 85% to about 95%. After the second serial addition, the conversion of the phosphorochloridite in the second reaction mixture can be about 95% to about 99%. The third serial addition can include water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH in sufficient quantity such that the conversion of the phosphorochloridite in the final reaction mixture is about 100%.

Forecasting

**[00134]** In various embodiments, using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of the X-OH to add in the second serial addition can include a forecasting process. The forecasting can be any suitable forecasting, wherein the amount of X-OH to add in the second addition is sufficient to create as much DLS as possible and to consume as much phosphorochloridite as possible without causing the levels of a side-product to exceed a pre-determined limit for that side-product in the final reaction mixture. Following the second addition, the remainder of the phosphorochloridite in the second reaction mixture (if any, e.g. if the second reaction mixture is not the final reaction mixture) can be consumed using an addition of water or by addition of the alcohol having the structure $R^1$-OH or $R^2$-OH. If a third addition is used, the quantity of water or alcohol to add in the third addition to consume the reminder of the phosphorochloridite can be estimated using any suitable method, such as using the selectivity ratios at various conversion ranges as described below.

**[00135]** The forecasting process can include using at least one selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range to forecast a maximum percent conversion of phosphorochloridite such that at the forecasted percent conversion in the second reaction mixture the percent of phosphorus present as CLS in the second reaction mixture is less than the pre-determined limit for the percent of phosphorus present as CLS in the final reaction mixture. The forecasting process can further include setting the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to the forecasted maximum percent conversion of the phosphorochloridite. The forecasting process can further include adding an amount of the X-OH in the second serial addition sufficient to cause the percent conversion of the phosphorochloridite in the second reaction mixture to be about equal to the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture.

**[00136]** In some embodiments, the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range includes a molar selectivity ratio of CLS to phosphorus-containing ligand of about 1:6 for conversions up to about 98%, for example for a conversions of about 90% to about 98%. In some examples, the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range includes a molar selectivity ratio of CLS to phosphorus-containing ligand of about 1:1 for conversions of between about 98% and about 100%.

**[00137]** In embodiments, the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range can occur at any suitable conversion range. For example, the conversion range of the phosphorochloridite can be about 0% to about 20%, about 0% to about 50%, about 0% to about 90%, about 0% to about 95%, about 0% to about 100%, about 20% to about 40%, about 40% to about 60%, about 60% to about 80%, or about 80% to about 100%. In embodiments, the selectivity ratio at the given conversion range can be any suitable selectivity ratio, for example, the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range can be about 1:(0.001-1000), such as about 1:0.001, 1:0.01, 1:0.1, 1:1, 1:2, 1:4, 1:6, 1:8, 1:10, 1:12, 1:14, 1:16, 1:18, 1:20, 1:100, or about 1:1000 molar ratio. In some examples, the selectivity ratio can be experimentally determined.

**[00138]** In some embodiments, a forecasting process can include using at least one selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and TLS at a given conversion range to forecast a maximum percent conversion of phosphorochloridite such that at the forecasted percent conversion in the second reaction mixture the percent of phosphorus present as TLS in the second reaction mixture is less than the pre-determined limit for the percent of phosphorus present as TLS in the final reaction mixture. The forecasting process can further include setting the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to the forecasted maximum percent conversion of the phosphorochloridite. The forecasting process can further include adding an amount of the X-OH in the second serial addition sufficient to cause the percent conversion of the phosphorochloridite in the second reaction mixture to be about equal to the pre-determined goal for the percent conversion of the phosphorochloridite in the second reaction mixture.

**[00139]** In some embodiments, the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and TLS at a given conversion range includes a molar selectivity ratio of TLS to phosphorus-containing ligand of about 1:6 for conversions up to about 98%, for example for a conversion of about 90% to about 98%. In some examples, the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and TLS at a given conversion range includes a molar selectivity ratio of TLS to phosphorus-containing ligand of about 1:1 for conversions of between about 98% and about 100%.

**[00140]** In embodiments, the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and TLS at a given conversion range can occur at any suitable conversion range. For example, the conversion range of the phosphorochloridite can be about 0% to about 20%, about 0% to about 50%, about 0% to about 90%, about 0% to about 95%, about 0% to about 100%, about 20% to about 40%, about 40% to about 60%, about 60% to about 80%, or about 80% to about 100%. In embodiments, the selectivity ratio at the given conversion range can be any suitable selectivity ratio, for example, the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and TLS at a given conversion range can be about 1:(0.001-100), such as about 1:0.001, 1:0.01, 1:0.1, 1:1, 1:2, 1:4, 1:6, 1:8, 1:10, 1:12, 1:14, 1:16, 1:18, 1:20, 1:100, or about 1:1000 molar ratio. In some examples, the selectivity ratio can be experimentally determined.

Reproducability

**[00141]** In some embodiments of the present invention, the impurity levels or yield of the final reaction mixture are highly reproducible within tight tolerances. This can be a major advantage of the present invention over other methods of making phosphorus-containing ligands.

**[00142]** For example, in some embodiments, the percent yield of the phosphorus-containing ligand between repetitions of the method is within 5%. In various embodiments, the percent yield of the phosphorus-containing ligand between repetitions can consistently be within 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%. For consistency, the tolerance can be achieved 2, 3, 4, 5, 10, 15, 20, 40, 60, 80, 100, 500, or over 1000 times without failure.

**[00143]** In some embodiments, the percentage of phosphorus present as TLS in the final product mixture is within 5% of the percentage of phosphorus present as TLS between repetitions of the method. In various embodiments, the percentage of phosphorus present as TLS in the final product mixture between repetitions can consistently be within 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%. For consistency, the tolerance can be achieved 2, 3, 4, 5, 10, 15, 20, 40, 60, 80, 100, 500, or over 1000 times without failure.

**[00144]** In some embodiments, the percentage of phosphorus preset as CLS in the final product mixture is within 5% of the percentage of phosphorus present as CLS between repetitions of the method. In various embodiments, the percentage of phosphorus present as TLS in the final product mixture between repetitions can consistently be within 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%. For consistency, the tolerance can be achieved 2, 3, 4, 5, 10, 15, 20, 40, 60, 80, 100, 500, or over 1000 times without failure.

**[00145]** In some embodiments, the percentage of phosphorus preset as LHP in the final product mixture is within 5% of the percentage of phosphorus present as LHP between repetitions of the method. In various embodiments, the percentage of phosphorus present as TLS in the final product mixture between repetitions can consistently be within 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%, 20%, 25%. For consistency, the tolerance can be achieved 2, 3, 4, 5, 10, 15, 20, 40, 60, 80, 100, 500, or over 1000 times without failure.

**[00146]** In some embodiments, any one or any combination of tolerances for various side-products or yields can be achieved.

## EXAMPLES

**[00147]** The present invention can be better understood by reference to the following examples which are offered by way of illustration. The present invention is not limited to the examples given herein.

**[00148]** The equipment used in the Examples that follow was a glass-lined reactor (nominal capacity about 630 L, inside diameter about 1,000 mm, jacket surface area about 3.2 $m^2$), impellor (about 480 mm diameter, 4 pitched-blades, downward pumping, maximum agitator speed 188 rpm), 2 finger baffles at opposite sides of reactor, 2 separate feeds pipes positioned near the impellor tip (4 mm diameter polytetrafluoroethylene (PTFE) tubes inside the finger baffles), sample withdrawal system, and a thermocouple (inside a finger baffle). There were no metallic components in contact with the fluid, glass-lined reactor, glass-coated agitator and baffles, or PTFE feed tubes.

**[00149]** During operation, the feeds were dosed to the reactor using manually controlled, positive displacement, piston pumps, with adjustments based on loss in weight (weigh scales). During dosage, the reaction mixture was stirred and the reaction temperature was controlled at about 50°C by the use of jacket cooling.

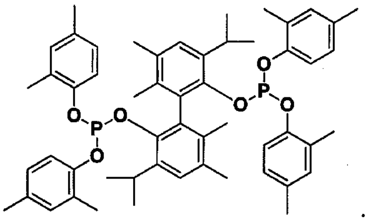
**[00150]** In the Examples that follow, the process goal was to maximise DLS yield while limiting amounts of side-products in the final reaction mixture to a maximum of about 3 molar percent of phosphorus present as CLS and to a maximum of about 3 molar percent of phosphorus present as LHP.

**[00151]** In all the Examples, the phosphorochloridite starting mixture was generated using a method similar to that described by PCT Publication WO 2004/050588. To a mixture of phosphorus trichloride (25 kg) in toluene (300 kg) was added 2,4-xylenol (45.5 kg) and triethylamine (39 kg) with stirring at about 50°C.

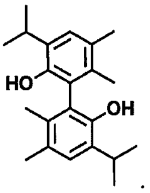
**[00152]** In all the Examples, the following procedure was used: (a) Phosphorus Nuclear Magnetic Resonance Spectroscopy ($^{31}$P NMR) was used to determine the phosphorus distribution of the starting mixture and this analysis was used to calculate the first serial dose of triethylamine and bis-aryl compound, to target about 90% phosphorochloridite conversion in the first reaction mixture. (b) After the first serial dose, $^{31}$P NMR was used to determine the phosphorus distribution of the first reaction mixture and this analysis was used to calculate (e.g. forecast) the second serial dose of bisaryl compound to limit CLS content in the second reaction mixture to a maximum of about 3 molar percent phosphorus (e.g. to add as much bisaryl as possible without causing the CLS content in the second reaction mixture to excess the pre-determined limit for CLS content in the final reaction mixture). (c) After the second serial addition to give the second reaction mixture, phosphorochloridite conversion was completed by adding the third addition, a small excess of 2,4-xylenol, to the second reaction mixture to give the final reaction mixture. In every case, the option of adding water to the second reaction mixture, instead of 2,4-xylenol, to complete phosphorochloridite conversion was rejected since this would have exceeded the LHP concentration maximum (e.g. would have exceeded the pre-determined limit for LHP content in the final reaction mixture). (d) After the third addition, $^{31}$P NMR was used to determine the phosphorus distribution of the final product mixture and this analysis was used to confirm the process goal had been achieved.

**[00153]** In the following examples, particular selectivity ratios are used for various ranges of phosphorochloridite conversion. These are only examples of particular selectivity ratios for various ranges of conversion, other selectivity ratios can be used. In one example, particular selectivity ratios can be determined experimentally.

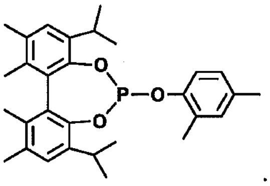
**[00154]** In the following examples, the DLS structure formed had the following chemical structure:



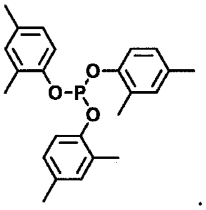
**[00155]** In the following examples, the bisaryl compound added had the following structure:



**[00156]** In the following examples, the CLS structure formed had the following structure:



**[00157]** In the following examples, the TLS structure formed had the following structure:



Example 1

Phosphorus Distribution – Starting Mixture

| Phosphorus Containing Component | Mol % P (approx) | Kg (approx) |
|---|---|---|
| DLS | 0 | 0 |
| TLS | 8 | 5.7 |
| CLS | 0 | 0 |
| Phosphorochloridite | 87 | 48.7 |
| LHP | 2 | |
| Other | 3 | |

**[00158]** First serial dose - To the stirred suspension was added a stoichiometric excess of triethylamine (20.3 kg) in one portion followed by bisaryl compound (22.3 kg) dissolved in toluene (36 wt%) dosed continuously over about 2 hours. The reaction mixture was then analysed by $^{31}$P NMR.

Phosphorus Distribution – First Reaction Mixture

| Phosphorus Containing Component | Mol % P (approx) | Kg (approx) |
|---|---|---|
| DLS | 69 | 54.7 |
| TLS | 14 | 10.1 |
| CLS | 2 | 1.7 |
| Phosphorochloridite | 10 | 5.6 |
| LHP | 3 | |
| Other | 2 | |

**[00159]** Second Serial dose - The second serial dose was calculated by running a by-product accumulation model. Using the selectivity ratio for the respective ranges of phosphorochloridite conversion, it was forecasted that molar percent of phosphorus present as CLS in the final reaction mixture would exceed 3% if the bisaryl addition continued to complete conversion of the phosphorochloridite.

Selectivity Ratios at Various Conversion Ranges

| | Molar Selectivity Ratio | | |
|---|---|---|---|
| Phosphorochloridite Conversion | DLS | CLS | TLS |
| 90% to 98% | 6 | 1 | 1 |
| 98% to 100% | 1 | 1 | 1 |

By-Product Accumulation Model

| Phosphorochloridite percent conversion | CLS (mol) | TLS (mol) |
|---|---|---|
| 10 | 2.00 | 14.00 |
| 9 | 2.13 | 14.13 |
| 8 | 2.25 | 14.25 |
| 7 | 2.38 | 14.38 |
| 6 | 2.50 | 14.50 |
| 5 | 2.63 | 14.63 |
| 4 | 2.75 | 14.75 |
| 3 | 2.88 | 14.88 |
| 2 | 3.00 | 15.00 |
| 1 | 3.33 | 15.33 |
| 0 | 3.67 | 15.67 |

**[00160]** To the stirred suspension was added a further quantity of bisaryl compound (2.7 kg) over about 60 minutes, targeting about 2% conversion of the phosphorochloridite in the second reaction mixture. This was followed by addition of a dose of 2,4-xylenol (0.5 kg) sufficient to complete the conversion of the phosphorochloridite, plus a small excess. The final reaction mixture was then analysed by $^{31}$P NMR.

Phosphorus Distribution – Final Reaction Mixture

| Phosphorus Containing Component | Mol % P (approx) | Kg (approx) |
|---|---|---|
| DLS | 76 | 60.3 |
| TLS | 16 | 11.5 |
| CLS | 3 | 2.6 |
| Phosphorochloridite | 0 | 0 |
| LHP | 2 | |
| Other | 3 | |

<u>Example 2</u>

Phosphorus Distribution – Starting Mixture

| Phosphorus Containing Component | Mol % P (approx) | Kg (approx) |
|---|---|---|
| DLS | 0 | 0 |
| TLS | 9 | 6.5 |
| CLS | 0 | 0 |
| Phosphorochloridite | 86 | 48.1 |
| LHP | 1 | |
| Other | 4 | |

**[00161]** First Serial Dose - To the stirred suspension was added a stoichiometric excess of triethylamine (22 kg) in one portion and bisaryl compound (22.8 kg) dissolved in toluene (30.5 wt%) dosed continuously over about 2 hours. The reaction mixture was then analysed by $^{31}P$ NMR.

Phosphorus Distribution – First Reaction Mixture

| Phosphorus Containing Component | Mol % P (approx) | Kg (approx) |
|---|---|---|
| DLS | 68 | 53.9 |
| TLS | 15 | 10.5 |
| CLS | 2.4 | 2.1 |
| Phosphorochloridite | 10.3 | 5.6 |
| LHP | 2.3 | |
| Other | 2 | |

**[00162]** Second Serial Dose - It was forecasted that the percentage of phosphorus present as CLS in the second reaction mixture would reach 3% at about 95% phosphorochloridite conversion.

Selectivity Ratios at Various Conversion Ranges

| | Molar Selectivity Ratio | | |
|---|---|---|---|
| Phosphorochloridite Conversion | DLS | CLS | TLS |
| 90% to 98% | 6 | 1 | 1 |
| 98% to 100% | 1 | 1 | 1 |

By-Product Accumulation Model

| Phosphorochloridite percent conversion | CLS (mol) | TLS (mol) |
|---|---|---|
| 10 | 2.40 | 14.60 |
| 9 | 2.53 | 14.73 |
| 8 | 2.65 | 14.85 |
| 7 | 2.78 | 14.98 |
| 6 | 2.90 | 15.10 |
| 5 | 3.03 | 15.23 |
| 4 | 3.15 | 15.35 |
| 3 | 3.28 | 15.48 |
| 2 | 3.40 | 15.60 |
| 1 | 3.73 | 15.93 |
| 0 | 4.07 | 16.27 |

**[00163]** To the stirred suspension was added a further quantity of bisaryl compound (2.5 kg) over about 60 minutes, targeting about 5% phosphorochloridite conversion, followed by a small dose of 2,4-xylenol (0.9 kg). The final reaction mixture was then analysed by $^{31}$P NMR.

Phosphorus Distribution – Final Product Mixture

| Phosphorus Containing Component | Mol % P (approx) | Kg (approx) |
|---|---|---|
| DLS | 75 | 57.1 |
| TLS | 19 | 14.4 |
| CLS | 3 | 2.6 |
| Phosphorochloridite | 0 | 0 |
| LHP | 2 | |
| Other | 1 | |

Example 3

Phosphorus Distribution – Starting Mixture

| Phosphorus Containing Component | Mol % P (approx) | Kg (approx) |
|---|---|---|
| DLS | 0 | 0 |
| TLS | 11.4 | 8.3 |
| CLS | 0 | 0 |
| Phosphorochloridite | 81 | 45.6 |
| LHP | 3.6 | |
| Other | 4 | |

**[00164]** First Serial Dose - To the stirred suspension was added a stoichiometric excess of triethylamine (21 kg) in one portion and bisaryl compound (22.3 kg) dissolved in toluene (35.4 wt%) dosed continuously over about 2 hours. The first reaction mixture was then analysed by $^{31}$P NMR.

Phosphorus Distribution – First Reaction Mixture

| Phosphorus Containing Component | Mol % P (approx) | Kg (approx) |
|---|---|---|
| DLS | 66.6 | 52.8 |
| TLS | 13.3 | 9.5 |
| CLS | 2 | 1.7 |
| Phosphorochloridite | 11.8 | 6.6 |
| LHP | 2.6 | |
| Other | 3.7 | |

**[00165]** Second Serial Dose - It was forecasted that the molar percentage of phosphorus present as CLS in the second reaction mixture would reach about 3% at about 96% phosphorochloridite conversion.

Selectivity Ratios at Various Conversion Ranges

| | Molar Selectivity Ratio | | |
|---|---|---|---|
| Phosphorochloridite Conversion | DLS | CLS | TLS |
| 90% to 98% | 6 | 1 | 1 |
| 98% to 100% | 1 | 1 | 1 |

By-Product Accumulation Model

| Phosphorochloridite percent conversion | CLS (mol) | TLS (mol) |
|---|---|---|
| 11.8 | 2.00 | 13.30 |
| 10 | 2.23 | 13.53 |
| 9 | 2.35 | 13.65 |
| 8 | 2.48 | 13.78 |
| 7 | 2.60 | 13.90 |
| 6 | 2.73 | 14.03 |
| 5 | 2.85 | 14.15 |
| 4 | 2.98 | 14.28 |
| 3 | 3.10 | 14.40 |
| 2 | 3.43 | 14.73 |
| 1 | 3.77 | 15.07 |
| 0 | 4.10 | 15.40 |

**[00166]** To the stirred suspension was added a further quantity of bisaryl compound (2.7 kg) over about 60 minutes, targeting about 4% phosphorochloridite conversion in the second reaction mixture, followed by a small dose of 2,4-xylenol (1.0 kg). The final reaction mixture was then analysed by $^{31}$P NMR.

Phosphorus Distribution – Final Product Mixture

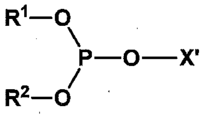
| Phosphorus Containing Component | Mol % P (approx) | Kg (approx) |
|---|---|---|
| DLS | 71.5 | 56.3 |
| TLS | 20.5 | 14.1 |
| CLS | 3.4 | 2.9 |
| Phosphorochloridite | 0 | 0 |
| LHP | 2.6 | |
| Other | 2 | |

**[00167]** The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments and optional features, modification and variation of the concepts herein disclosed can be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the appended claims.

Additional Embodiments.

**[00168]** The present invention provides for the following exemplary embodiments, the numbering of which is not to be construed as designating levels of importance:

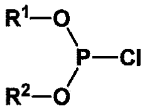
**[00169]** Embodiment 1 provides a method for producing a phosphorus-containing ligand structure having the following chemical structure



**Structure I'**

including:

contacting a phosphorochloridite of the following structure,



**Structure II**

with a compound having the chemical structure X-OH and a tertiary organic amine to provide a final reaction mixture including the ligand structure;

wherein the contacting includes

providing a pre-determined limit for a mole percent of phosphorus present as at least one side-product in the final reaction mixture;

adding the X-OH to the phosphorochloridite in a first serial addition, to provide a first reaction mixture;

determining a mole percent of phosphorus present in the first reaction mixture as the at least one side-product;

using a comparison of the mole percent of phosphorus present in the first reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and an alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a second serial addition;

adding the second serial addition to the first reaction mixture, including a compound selected from the group consisting of the X-OH, water, or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide a second reaction mixture; and

either

performing third addition steps including

optionally determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product;

optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition; and

adding the third serial addition to the second reaction mixture, including a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture;

or

the final reaction mixture is the second reaction mixture;

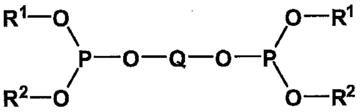
wherein in Structures I' and II, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; $R^1$ and $R^2$ are bridged to one another or unbridged to one another; and each of X and X' are independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, phosphitylbisaryl, phosphitylbisheteroaryl, hydroxybisaryl, hydroxybisheteroaryl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups.

**[00170]** Embodiment 2 provides the method of Embodiment 1, wherein third addition steps are performed and further include:

determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product; and

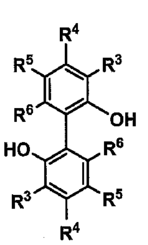
using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition.

**[00171]** Embodiment 3 provides the method of any one of Embodiments 1-2, wherein the ligand structure of Structure I' is a diphosphite ligand structure (DLS) having the chemical structure of Structure I,

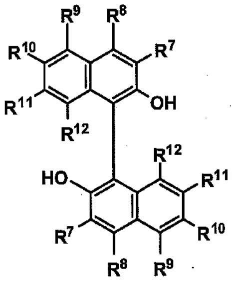


**Structure I**

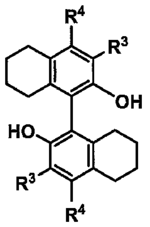
wherein the X-OH is a bisaryl compound selected from the group consisting of Structure III, Structure IV, and Structure V,



**Structure III**



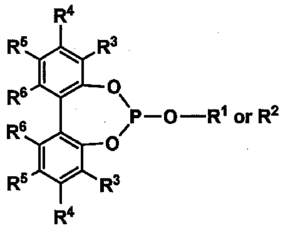
**Structure IV**



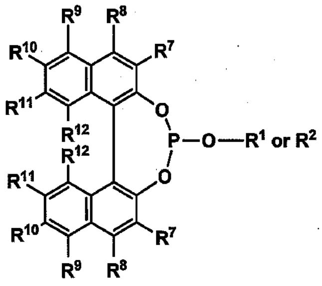
**Structure V;**

wherein in Structures I-V, R$^1$ and R$^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; each of R$^3$, R$^4$, R$^5$, R$^6$, R$^7$, R$^8$, R$^9$, R$^{10}$, R$^{11}$, and R$^{12}$ is independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups; and O-Q-O is a divalent species of the bisaryl compound.

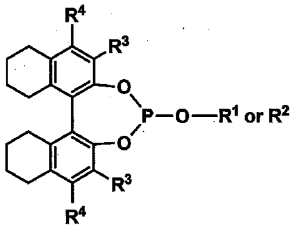
[00172] Embodiment 4 provides the method of any one of Embodiments 1-3, wherein the at least one side-product includes a C-phite ligand structure (CLS), having the chemical structure shown below as Structure VI, VII, or VIII,



**Structure VI**



**Structure VII**



**Structure VIII**

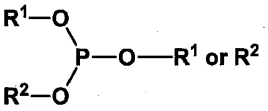
wherein in Structures VI-VIII, R$^1$ and R$^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; R$^1$ and R$^2$ are bridged to one another or unbridged to one another; and each of R$^3$, R$^4$, R$^5$, R$^6$, R$^7$, R$^8$, R$^9$, R$^{10}$, R$^{11}$, and R$^{12}$ is independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups;

wherein providing a pre-determined limit for the mole percent of phosphorus present as at least one side-product in the final reaction mixture includes providing a pre-determined limit for a mole percent of phosphorus present as CLS in the final reaction mixture.

**[00173]** Embodiment 5 provides the method of Embodiment 4, wherein in the final reaction mixture, the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 65%, and the percentage of phosphorus present as the CLS is less than about 5%.

**[00174]** Embodiment 6 provides the method of any one of Embodiments 4-5, wherein in the final reaction mixture, the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 70%, and the percentage of phosphorus present as the CLS is less than about 3.5%.

**[00175]** Embodiment 7 provides the method of any one of Embodiments 1-6, wherein the at least one side-product includes a T-phite ligand structure (TLS), having the chemical structure shown below as Structure IX,

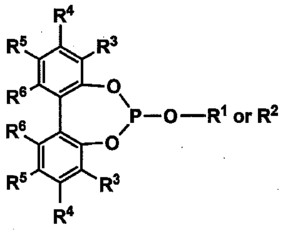


**Structure IX;**

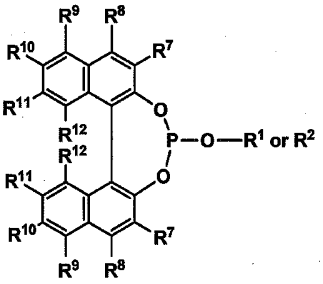
wherein in Structure IX, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; and $R^1$ and $R^2$ are bridged to one another or unbridged to one another;

wherein providing a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture includes providing a pre-determined limit for a mole percent of phosphorus present as TLS in the final reaction mixture.

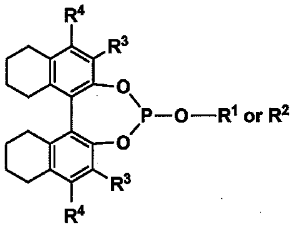
**[00176]** Embodiment 8 provides the method of any one of Embodiments 1-7, wherein the at least one side-product includes a C-phite ligand structure (CLS), having the chemical structure shown below as Structure VI, VII, or VIII,



Structure VI

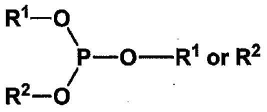


Structure VII



Structure VIII;

wherein the at least one side-product further includes a T-phite ligand structure (TLS), having the chemical structure shown below as Structure IX,



Structure IX;

wherein in Structures VI-VIII and IX, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; $R^1$ and $R^2$ are bridged to one another or unbridged to one another; and each of $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ is independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups;

wherein providing a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture includes providing a pre-determined limit for a mole percent of phosphorus present as TLS in the final reaction mixture;

wherein providing a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture includes providing a pre-determined limit for a mole percent of phosphorus present as CLS in the final reaction mixture.

**[00177]** Embodiment 9 provides the method of any one of Embodiments 1-8, wherein the at least one side-product includes a ligand hydrolysis product (LHP), including a product derived by a process including

hydrolysis of the phosphorus-containing ligand or of the phosphorochloridite;

hydrolysis of a product derived from the phosphorus-containing ligand or from the phosphorochloridite; or

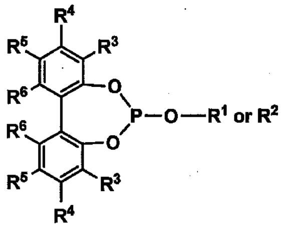
reaction of the hydrolysis product of the phosphorus-containing ligand or of the phosphorochloridite, or reaction of the hydrolysis product of a product derived from the phosphorus-containing ligand or from the phosphorochloridite;

wherein providing a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture includes providing a pre-determined limit for a mole percent of phosphorus present as LHP in the final reaction mixture.

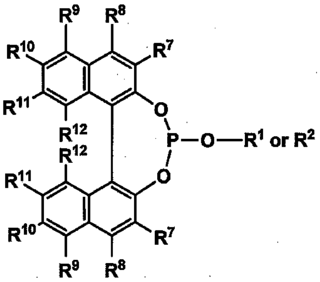
**[00178]** Embodiment 10 provides the method of Embodiment 9, wherein in the final reaction mixture, the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 65%, and the percentage of phosphorus present as the LHP is less than no more than about 5%.

**[00179]** Embodiment 11 provides the method of any one of Embodiments 9-10, wherein in the final reaction mixture, the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 70%, and the percentage of phosphorus present as the LHP is less than no more than about 3.5%.

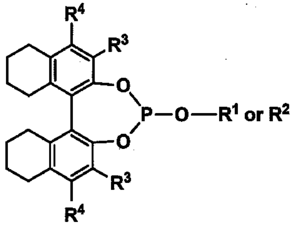
**[00180]** Embodiment 12 provides the method of any one of Embodiments 1-11, wherein the at least one side-product includes a C-phite ligand structure (CLS), having the chemical structure shown below as Structure VI, VII, or VIII,



Structure VI

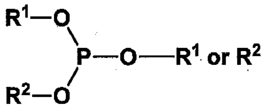


Structure VII



Structure VIII;

wherein the at least one side-product further includes a T-phite ligand structure (TLS), having the chemical structure shown below as Structure IX,



Structure IX;

wherein in Structures VI-VIII and IX, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; $R^1$ and $R^2$ are bridged to one another or unbridged to one another; and each of $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ is independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups;

wherein providing a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture includes providing a pre-determined limit for a mole percent of phosphorus present as TLS in the final reaction mixture;

wherein providing a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture includes providing a pre-determined limit for a mole percent of phosphorus present as CLS in the final reaction mixture;

wherein the at least one side-product further includes a ligand hydrolysis product (LHP), including a product derived by a process including

hydrolysis of the phosphorus-containing ligand or of the phosphorochloridite;

hydrolysis of a product derived from the phosphorus-containing ligand or from the phosphorochloridite; or

reaction of the hydrolysis product of the phosphorus-containing ligand or of the phosphorochloridite, or reaction of the hydrolysis product of a product derived from the phosphorus-containing ligand or from the phosphorochloridite;

wherein providing a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture includes providing a pre-determined limit for a mole percent of phosphorus present as LHP in the final reaction mixture.

**[00181]** Embodiment 13 provides the method of any one of Embodiments 1-12, wherein the contacting further includes using the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture to determine an amount of the X-OH to add in the first or second serial addition to cause a mole percent of phosphorus present in the first or second reaction mixtures as the at least one side-product to be less than the pre-determined limit of the mole percent of phosphorus present as the at least one side-product in the final reaction mixture.

**[00182]** Embodiment 14 provides the method of any one of Embodiments 2-13, wherein the contacting further includes using the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture to determine an amount of the X-OH to add in the third serial addition to cause a mole percent of phosphorus present in the final reaction mixture as the at least one side-product to be less than the pre-determined limit of the mole percent of phosphorus present as the at least one side-product in the final reaction mixture.

**[00183]** Embodiment 15 provides the method of any one of Embodiments 1-14, wherein the amount of the X-OH added in the second serial addition is less than the amount of the X-OH added in the first serial addition; and wherein the amount of the X-OH added in the third serial addition if performed is equal to or less than the amount of the X-OH added in the second serial addition.

**[00184]** Embodiment 16 provides the method of Embodiment 1, wherein the amount of the X-OH added in the second or third serial addition is none.

**[00185]** Embodiment 17 provides the method of any one of Embodiments 1-16, wherein if the amount of the X-OH added in the second serial addition is none, then the second serial addition includes at least one of water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and wherein if the amount of the X-OH added in the third serial addition is none, then the third serial addition if performed includes at least one of water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00186]** Embodiment 18 provides the method of any one of Embodiments 4-17, wherein using a comparison of the mole percent of phosphorus present in the first or second reaction mixture as the CLS to the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture to determine the amount of a compound to add in the second serial addition or the third serial addition if performed includes adding an amount of a compound in the second or third addition selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH sufficient to cause the mole percent of phosphorus in the second or final reaction mixture present as the CLS to be equal to or below the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture.

**[00187]** Embodiment 19 provides the method of Embodiment 18, wherein if the mole percent of phosphorus present in the first reaction mixture as the CLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, then the second serial addition includes water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and wherein if the mole percent of phosphorus present in the second reaction mixture as the CLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, then the third serial addition if performed includes water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00188]** Embodiment 20 provides the method of any one of Embodiments 18-19, wherein if the mole percent of phosphorus present in the first reaction mixture as the CLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, then the second serial addition does not include the X-OH; and wherein if the mole percent of phosphorus present in the second reaction mixture as the CLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, then the third addition if performed does not include the X-OH.=

**[00189]** Embodiment 21 provides the method of any one of Embodiments 7-20, wherein using a comparison of the mole percent of phosphorus present in the first or second reaction mixture as the TLS to the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture to determine the amount of a compound to add in the second or third serial addition includes adding an amount of a compound in the second or third addition selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH sufficient to cause the mole percent of phosphorus in the second or final reaction mixture present as the TLS to be equal to or below the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture.

**[00190]** Embodiment 22 provides the method of Embodiment 21, wherein if the mole percent of phosphorus present in the first reaction mixture as the TLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the second serial addition includes water; and wherein if the mole percent of phosphorus present in the second reaction mixture as the TLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the third serial addition if performed includes water.

**[00191]** Embodiment 23 provides the method of any one of Embodiments 21-22, wherein if the mole percent of phosphorus present in the first reaction mixture as TLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the second serial addition does not include the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and wherein if the mole percent of phosphorus present in the second reaction mixture as TLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the third serial addition if performed does not include the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00192]** Embodiment 24 provides the method of any one of Embodiments 9-23, wherein using a comparison of the mole percent of phosphorus present in the first or second reaction mixture as the LHP to the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture to determine the amount of a compound to add in the second or third serial addition includes adding an amount of a compound in the second or third addition selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH sufficient to cause the mole percent of phosphorus in the second or final reaction mixture present as the LHP to be equal to or below the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture.

**[00193]** Embodiment 25 provides the method of Embodiment 24, wherein if the mole percent of phosphorus present in the first reaction mixture as LHP is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture, then the second serial addition includes the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and wherein if the mole percent of phosphorus present in the second reaction mixture as LHP is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture, then the third serial addition if performed includes the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00194]** Embodiment 26 provides the method of any one of Embodiments 24-25, wherein if the mole percent of phosphorus present in the first reaction mixture as LHP is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture, then the second serial addition does not include water; and wherein if the mole percent of phosphorus present in the second reaction mixture as LHP is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture, then the third serial addition if performed does not include water.

**[00195]** Embodiment 27 provides the method of any one of Embodiments 8-26, wherein if in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition includes water; and wherein if in the second reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the third serial addition if performed includes water.

**[00196]** Embodiment 28 provides the method of any one of Embodiments 8-27, wherein if in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition does not include the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and wherein if in the second reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then if performed the third serial addition does not include the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00197]** Embodiment 29 provides the method of any one of Embodiments 1-28, wherein the contacting further includes:

providing a pre-determined goal for a conversion of phosphorochloridite in the second reaction mixture;

after adding the first serial addition, determining the percent conversion of the phosphorochloridite in the first reaction mixture; and

before adding the second serial addition, using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of the X-OH to add in the second serial addition.

**[00198]** Embodiment 30 provides the method of any one of Embodiments 8-29, wherein the contacting further includes:

providing a pre-determined goal for a conversion of phosphorochloridite in the second reaction mixture;

after adding the first serial addition, determining the percent conversion of the phosphorochloridite in the first reaction mixture; and

before adding the second serial addition, using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of the X-OH to add in the second serial addition.

**[00199]** Embodiment 31 provides the method of Embodiment 30, wherein if in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor as the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or as the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction mixture is less than the pre-determined goal for the conversion of phosphorochloridite in the final reaction mixture, then the amount of the X-OH to add in the second serial addition is sufficient to make the percent conversion of the phosphorochloridite in the second reaction mixture equal to or above the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture.

**[00200]** Embodiment 32 provides the method of any one of Embodiments 30-31, wherein if in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor as the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or as the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction mixture is less than the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture, then the second serial addition does not include water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00201]** Embodiment 33 provides the method of any one of Embodiments 1 or 29, wherein if percent conversion of the phosphorochloridite in the second reaction mixture is less than about 100%, then further including adding the third serial addition to the second reaction mixture, wherein the third serial addition includes a sufficient quantity of water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH such that following the third serial addition the phosphorochloridite conversion in the final reaction mixture is about 100%.

**[00202]** Embodiment 34 provides the method of any one of Embodiments 7-33, further including determining the percent conversion of the phosphorochloridite in the second reaction mixture and determining the mole percent of phosphorus present as TLS in the second reaction mixture, wherein if percent conversion of the phosphorochloridite in the second reaction mixture is less than about 100%, and if in the second reaction mixture the mole percent of phosphorus present as TLS is less than the pre-determined limit for the mole percent of phosphorus present as TLS in the final reaction mixture, then further including adding the third serial addition to the second reaction mixture, wherein the third serial addition includes a sufficient quantity of the alcohol having the chemical structure $R^1$-OH or $R^2$-OH such that following the third serial addition the conversion of the phosphorochloridite in the final reaction mixture is about 100%.

**[00203]** Embodiment 35 provides the method of any one of Embodiments 9-34, wherein if percent conversion of the phosphorochloridite in the second reaction mixture is less than about 100%, and if in the second reaction mixture the mole percent of phosphorus present as LHP is less than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then further including adding a third serial addition to the second reaction mixture, wherein the third serial addition includes a sufficient quantity of water such that following the third serial addition the conversion of the phosphorochloridite in the final reaction mixture is about 100%.

**[00204]** Embodiment 36 provides the method of Embodiment 35, wherein following the third serial addition, in the final reaction mixture the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 65% and the percentage of phosphorus present as the LHP is less than about 5%.

**[00205]** Embodiment 37 provides the method of any one of Embodiments 35-36, wherein following the third serial addition, in the final reaction mixture the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 70%, and the percentage of phosphorus present as the LHP is less than about 3.5%.

**[00206]** Embodiment 38 provides the method of any one of Embodiments 1-37, wherein the contacting further includes:

providing a pre-determined goal for a conversion of phosphorochloridite in the first reaction mixture;

before adding the first serial addition, using the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture to determine the amount of the X-OH to add in the first serial addition, such that the conversion of phosphorochloridite in the first reaction mixture is at or above the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture.

**[00207]** Embodiment 39 provides the method of any one of Embodiments 9-38, wherein the contacting further includes:

providing a pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture;

after adding the first serial addition, determining the mole percent of phosphorus present as LHP in the first reaction mixture; and

before adding the second serial addition, using a comparison of the mole percent of phosphorus present as LHP in the first reaction mixture to the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture to determine the composition of the second serial addition.

**[00208]** Embodiment 40 provides the method of any one of Embodiments 12-39, wherein the contacting further includes:

providing a pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture;

after adding the first serial addition, determining the mole percent of phosphorus present as LHP in the first reaction mixture; and

before adding the second serial addition, using a comparison of the mole percent of phosphorus present as LHP in the first reaction mixture to the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture to determine the composition of the second serial addition.

**[00209]** Embodiment 41 provides the method of Embodiment 40, wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition includes the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00210]** Embodiment 42 provides the method of any one of Embodiments 40-41, wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the

TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition does not include the X-OH or water.

**[00211]** Embodiment 43 provides the method of any one of Embodiments 8-42, wherein the contacting further includes:

providing a pre-determined goal for a conversion of phosphorochloridite in the second reaction mixture; and

after adding the first serial addition,

determining the percent conversion of the phosphorochloridite in the first reaction mixture; and

wherein if in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition includes water;

wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the second serial addition includes water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and

wherein if in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor as the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction product is less than the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture, then the second serial includes a sufficient amount of the X-OH such that the percent conversion of the phosphorochloridite in the second reaction mixture is equal to or above the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture.

**[00212]** Embodiment 44 provides the method of Embodiment 43, wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the second serial addition includes the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00213]** Embodiment 45 provides the method of any one of Embodiments 12-44, wherein the contacting further includes:

providing a pre-determined goal for a conversion of phosphorochloridite in the second reaction mixture; and

after adding the first serial addition,

determining the percent conversion of the phosphorochloridite in the first reaction mixture; and

determining the mole percent of phosphorus present as LHP in the first reaction mixture;

wherein if in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition includes water;

wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition includes the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and

wherein if in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction product is less than the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture, then second serial addition includes X-OH in sufficient quantity such that the percent conversion of the phosphorochloridite in the second reaction mixture is equal to or above the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture.

**[00214]** Embodiment 46 provides the method of Embodiment 45, wherein contacting further includes:

wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is not equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition includes water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and

wherein if in the first reaction mixture the mole percent of phosphorus present as the TLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the CLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is not equal or to greater than the pre-determined limit for LHP content in the final reaction mixture, then the second addition includes water.

**[00215]** Embodiment 47 provides the method of any one of Embodiments 45-46, wherein contacting further includes:

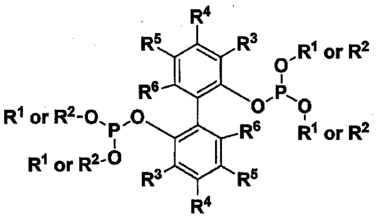
wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is not equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition does not include the X-OH; and

wherein if in the first reaction mixture the mole percent of phosphorus present as the TLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the CLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is not equal or to greater than the pre-determined limit for LHP content in the final reaction mixture, then the second addition does not include water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

**[00216]** Embodiment 48 provides the method of any one of Embodiments 1-47, wherein the first reaction mixture has a stoichiometric excess of phosphorochloridite.

**[00217]** Embodiment 49 provides the method of any one of Embodiments 1-48, wherein the contacting is carried out in the presence of a stoichiometric excess of tertiary organic amine.

**[00218]** Embodiment 50 provides the method of any one of Embodiments 1-49, wherein the phosphorus-containing ligand has the following chemical structure:

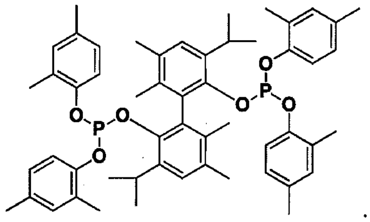


wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

**[00219]** Embodiment 51 provides the method of any one of Embodiments 1-50, wherein $R^2 = R^1$, wherein $R^1$ is a monovalent xylene group.

**[00220]** Embodiment 52 provides the method of any one of Embodiments 1-51, wherein $R^2 = R^1$, wherein $R^1$ is a monovalent 2,4-xylene group

**[00221]** Embodiment 53 provides the method of any one of Embodiments 1-52, wherein the phosphorus-containing ligand has the following chemical structure:



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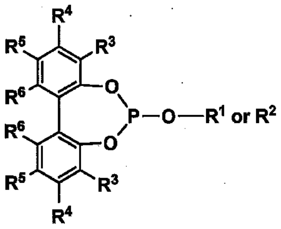
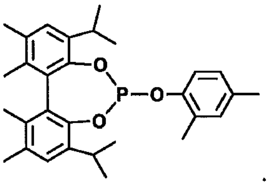
**[00222]** Embodiment 54 provides the method of any one of Embodiments 4-53, wherein the CLS has the following chemical structure:



wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

**[00223]** Embodiment 55 provides the method of any one of Embodiments 4-54, wherein the CLS has the following chemical structure:



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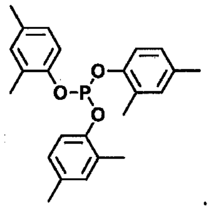
**[00224]** Embodiment 56 provides the method of any one of Embodiments 7-55, wherein the TLS has the chemical structure $P(OR^1)_3$, wherein $R^1$ is a substituted or unsubstituted aryl group.

**[00225]** Embodiment 57 provides the method of any one of Embodiments 7-56, wherein the TLS has the following chemical structure:



**[00226]** Embodiment 58 provides the method of any one of Embodiments 1-57, wherein the tertiary organic amine includes a trialkylamine.

**[00227]** Embodiment 59 provides the method of any one of Embodiments 1-58, wherein the tertiary organic amine includes triethylamine.

**[00228]** Embodiment 60 provides the method of any one of Embodiments 4-59, wherein the pre-determined limit for the mole percent phosphorus present as the CLS in the final reaction mixture is less than or equal to about 5%.

**[00229]** Embodiment 61 provides the method of any one of Embodiments 4-60, wherein the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture is less than or equal to about 3%.

**[00230]** Embodiment 62 provides the method of any one of Embodiments 30, 43, or 45, wherein using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of the X-OH to add in the second serial addition includes:

using at least one selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range to forecast a maximum percent conversion of phosphorochloridite such that at the forecasted percent conversion in the second reaction mixture the percent of phosphorus present as CLS in the second reaction mixture is less than the pre-determined limit for the percent of phosphorus present as CLS in the final reaction mixture;

setting the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to the forecasted maximum percent conversion of the phosphorochloridite; and

adding an amount of the X-OH in the second serial addition sufficient to cause the percent conversion of the phosphorochloridite in the second reaction mixture to be about equal to the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture.

**[00231]** Embodiment 63 provides the method of Embodiment 62, wherein the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range includes a molar selectivity ratio of CLS to phosphorus-containing ligand of about 1:6 for conversions up to about 98%.

**[00232]** Embodiment 64 provides the method of any one of Embodiments 62-63, wherein the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range includes a molar selectivity ratio of CLS to phosphorus-containing ligand of about 1:1 for conversions of between about 98% and about 100%.

**[00233]** Embodiment 65 provides the method of any one of Embodiments 7-64, wherein the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture is less than or equal to about 30%.

**[00234]** Embodiment 66 provides the method of any one of Embodiments 7-65, wherein the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture is less than or equal to about 22%.

**[00235]** Embodiment 67 provides the method of any one of Embodiments 30, 43, or 45, wherein using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of the X-OH to add in the second serial addition includes:

using at least one selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and TLS at a given conversion range to forecast a maximum percent conversion of phosphorochloridite such that at the forecasted percent conversion in the second reaction mixture the percent of phosphorus present as TLS in the second reaction mixture is less than the pre-determined limit for the percent of phosphorus present as TLS in the final reaction mixture;

setting the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to the forecasted maximum percent conversion of the phosphorochloridite; and

adding an amount of the X-OH in the second serial addition sufficient to cause the percent conversion of the phosphorochloridite in the second reaction mixture to be about equal to the pre-determined goal for the percent conversion of the phosphorochloridite in the second reaction mixture.

**[00236]** Embodiment 68 provides the method of Embodiment 67, wherein the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range includes a molar selectivity ratio of CLS to phosphorus-containing ligand of about 1:6 for conversions up to about 98%.

**[00237]** Embodiment 69 provides the method of any one of Embodiments 67-68, wherein the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range includes a molar selectivity ratio of CLS to phosphorus-containing ligand of about 1:1 for conversions of between about 98% and about 100%.

**[00238]** Embodiment 70 provides the method of any one of Embodiments 29, 30, 43, or 45, wherein the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture is about 95% to about 100%.

**[00239]** Embodiment 71 provides the method of any one of Embodiments 29, 30, 43, or 45, wherein the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture is about 96% to about 99%.

**[00240]** Embodiment 72 provides the method of any one of Embodiments 38-71, wherein the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture is about 85% to about 95%.

**[00241]** Embodiment 73 provides the method of any one of Embodiments 38-72, wherein the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture is about 90%.

**[00242]** Embodiment 74 provides the method of any one of Embodiments 39, 40, or 45, wherein the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture is about 5%.

**[00243]** Embodiment 75 provides the method of any one of Embodiments 39, 40, or 45, wherein the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture is about 3%.

**[00244]** Embodiment 76 provides the method of any one of Embodiments 1-75, wherein the contacting is carried out by at least one step selected from the group consisting of

(i) feeding the X-OH to a mixture of the phosphorochloridite and the tertiary organic amine;

(ii) feeding the X-OH and the tertiary organic amine separately to the phosphorochloridite; or

(iii) feeding the X-OH and the tertiary organic amine as a mixture to the phosphorochloridite.

**[00245]** Embodiment 77 provides the method of any one of Embodiments 1-76 wherein the reaction mixture further includes at least one aromatic hydrocarbon solvent.

**[00246]** Embodiment 78 provides the method of Embodiment 77 wherein the aromatic solvent includes toluene.

**[00247]** Embodiment 79 provides the method of any one of Embodiments 77-78 further including feeding the X-OH to the phosphorochloridite as a solution including the X-OH and the hydrocarbon solvent.

**[00248]** Embodiment 80 provides the phosphorus-containing ligand of Structure I made by the method of any one of Embodiments 1-79.

**[00249]** Embodiment 81 provides the method of any one of Embodiments 1-80, wherein

the first serial addition includes the X-OH in sufficient quantity such that the conversion of the phosphorochloridite in the first reaction mixture is about 85% to about 95%; and

the second serial addition includes a smaller amount of the X-OH than the amount of the X-OH added in the first serial addition.

**[00250]** Embodiment 82 provides the method of any one of Embodiments 1-81, wherein

the first serial addition includes X-OH in sufficient quantity such that the conversion of the phosphorochloridite in the first reaction mixture is about 85% to about 90%; and

the second serial addition includes the alcohol having the chemical structure $R^1$-OH or $R^2$-OH in sufficient quantity such that in the second reaction mixture phosphorochloridite conversion is about 100%.

**[00251]** Embodiment 83 provides the method of any one of Embodiments 1-82, wherein

the first serial addition includes the X-OH in sufficient quantity such that the conversion of the phosphorochloridite in the first reaction mixture is about 85% to about 95%; and

after the second serial addition, the conversion of the phosphorochloridite in the second reaction mixture is about 95% to about 99%;

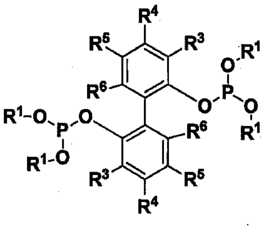
the third serial addition includes water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH in sufficient quantity such that the conversion of the phosphorochloridite in the final reaction mixture is about 100%.

**[00252]** Embodiment 84 provides the method of any one of Embodiments 1-83, wherein the method gives a final reaction mixture that is a first final reaction mixture, wherein the method is repeated to give a second final reaction mixture, wherein the yield of the phosphorus-containing ligand in the first final reaction mixture is within 5% of the yield of the phosphorus-containing ligand in the second final reaction mixture.

**[00253]** Embodiment 85 provides the method of any one of Embodiments 4-84, wherein the method gives a final reaction mixture that is a first final reaction mixture, wherein the method is repeated to give a second final reaction mixture, wherein the percentage of phosphorus in the first final reaction mixture present as the phosphorus-containing ligand, TLS, and CLS, is each within 5% of the percentage of phosphorus in the second final reaction mixture present as the phosphorus-containing ligand, TLS, and CLS, respectively.

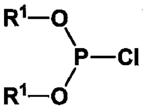
**[00254]** Embodiment 86 provides the method of any one of Embodiments 4-85, wherein the method gives a final reaction mixture that is a first final reaction mixture, wherein the method is repeated to give a second final reaction mixture, wherein the percentage of phosphorus in the first final reaction mixture present as CLS is within 5% of the percentage of phosphorus in the second final reaction mixture present as the CLS.

**[00255]** Embodiment 87 provides a method for producing a diphosphite ligand structure (DLS) having the following structure,

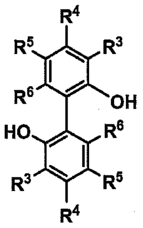


including:

contacting a phosphorochloridite having the following structure,



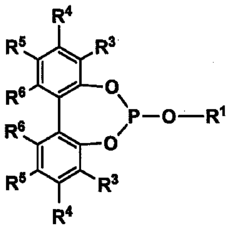
with a bisaryl compound having the following structure,



and a tertiary organic amine to provide a final reaction mixture including the diphosphite;

wherein the contacting includes

providing a pre-determined limit for the mole percent of phosphorus present as C-phite ligand structure (CLS), having the chemical structure shown below, in the final reaction mixture



adding the bisaryl compound to the phosphorochloridite in a first serial addition such that the moles of phosphorochloridite added in the first addition is greater than the number of moles of the bisaryl compound added in the first addition, to provide a first reaction mixture;

determining the mole percent of phosphorus present in the first reaction mixture as CLS;

using a comparison of the mole percent of phosphorus present in the first reaction mixture as CLS to the pre-determined limit for the mole percent of phosphorus present as CLS to determine an amount of a compound selected from the group consisting of at least one of the bisaryl compound, water, and an alcohol having the chemical structure $R^1$-OH, to add in a second serial addition such that the mole percent of phosphorus present as CLS in a second reaction mixture is less than or equal to the pre-determined limit for the mole percent of phosphorus present as CLS in the final reaction mixture;

adding the second serial addition to the first reaction mixture, including a compound selected from the group consisting of the bisaryl compound, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the second reaction mixture; and

either

performing third addition steps including

optionally determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product;

optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition; and

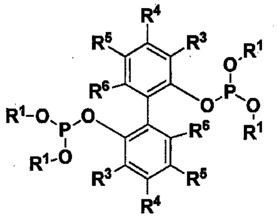
adding the third serial addition to the second reaction mixture, including a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture;

or

the final reaction mixture is the second reaction mixture;

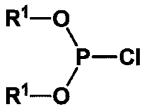
wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

**[00256]** Embodiment 88 provides a method for producing a diphosphite ligand structure (DLS) having the following structure,

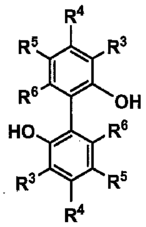


including:

contacting a phosphorochloridite having the following structure,



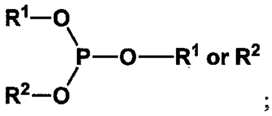
with a bisaryl compound having the following structure,



and a tertiary organic amine to provide a final reaction mixture including the diphosphite;

wherein the contacting includes

providing a pre-determined limit for the mole percent of phosphorus present as T-phite ligand structure (TLS), having the chemical structure shown below, in the final reaction mixture



;

adding the bisaryl compound to the phosphorochloridite in a first serial addition such that the moles of phosphorochloridite added in the first addition is greater than the number of moles of biaryl added in the first addition, to provide a first reaction mixture;

determining the mole percent of phosphorus present in the first reaction mixture as TLS;

using a comparison of the mole percent of phosphorus present in the first reaction mixture as TLS to the pre-determined limit for the mole percent of phosphorus present as TLS to determine an amount of a compound selected from the group consisting of the bisaryl compound, water, and an alcohol having the chemical structure $R^1$-OH, to add in a second serial addition such that the mole percent of phosphorus present as TLS in a second reaction mixture is less than or equal to the pre-determined limit for the mole percent of phosphorus present as TLS in the final reaction mixture;

adding the second serial addition to the first reaction mixture, including a compound selected from the group consisting of the bisaryl compound, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the second reaction mixture; and

either

performing third addition steps including

optionally determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product;

optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition; and

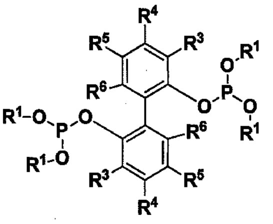
adding the third serial addition to the second reaction mixture, including a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture;

or

the final reaction mixture is the second reaction mixture;

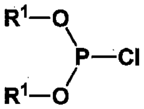
wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; and each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

[00257] Embodiment 89 provides a method for producing a diphosphite ligand structure (DLS) having the following structure,

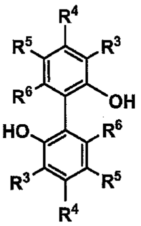


including:

contacting a phosphorochloridite having the following structure,



with a bisaryl compound having the following structure,



and a tertiary organic amine to provide a final reaction mixture including the diphosphite;

wherein the contacting includes

providing a pre-determined limit for the mole percent of phosphorus present as a ligand hydrolysis product (LHP) in the final reaction mixture, including a product derived by a process including hydrolysis of the DLS or of the phosphorochloridite;

hydrolysis of a product derived from the DLS or from the phosphorochloridite; or

reaction of the hydrolysis product of the DLS or of the phosphorochloridite, or reaction of the hydrolysis product of a product derived from the DLS or from the phosphorochloridite;

adding the bisaryl compound to the phosphorochloridite in a first serial addition such that the moles of phosphorochloridite added in the first addition is greater than the number of moles of biaryl added in the first addition, to provide a first reaction mixture;

determining the mole percent of phosphorus present in the first reaction mixture as LHP;

using a comparison of the mole percent of phosphorus present in the first reaction mixture as LHP to the pre-determined limit for the mole percent of phosphorus present as LHP to determine an amount of a compound selected from the group consisting of the bisaryl compound, water, and an alcohol having the chemical structure $R^1$-OH, to add in a second serial addition such that the mole percent of phosphorus present as LHP in a second reaction mixture is less than or equal to the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture;

adding the second serial addition to the first reaction mixture, including a compound selected from the group consisting of the bisaryl compound, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the second reaction mixture; and

either

performing third addition steps including

optionally determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product;

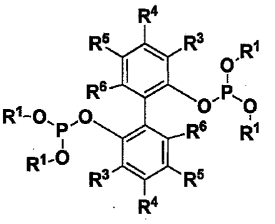
optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition; and adding the third serial addition to the second reaction mixture, including a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture;

or

the final reaction mixture is the second reaction mixture;

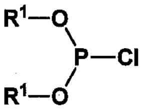
wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; and each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

**[00258]** Embodiment 90 provides a method for producing a diphosphite ligand structure (DLS) having the following structure,

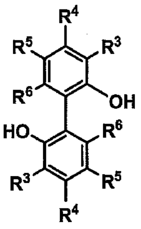


including:

contacting a phosphorochloridite having the following structure,



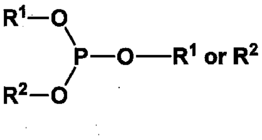
with a bisaryl compound having the following structure,



and a tertiary organic amine to provide a final reaction mixture including the diphosphite;

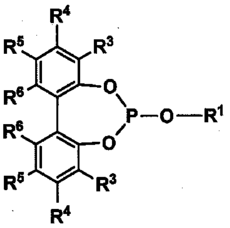
wherein the contacting includes

providing a pre-determined limit for the mole percent of phosphorus present as T-phite ligand structure (TLS), having the chemical structure shown below, in the final reaction mixture



;

providing a pre-determined limit for the mole percent of phosphorus present as C-phite ligand structure (CLS), having the chemical structure shown below, in the final reaction mixture



providing a pre-determined limit for the mole percent of phosphorus present as a ligand hydrolysis product (LHP) in the final reaction mixture, including a product derived by a process including

hydrolysis of the DLS or of the phosphorochloridite;

hydrolysis of a product derived from the DLS or from the phosphorochloridite; or

reaction of the hydrolysis product of the DLS or of the phosphorochloridite, or reaction of the hydrolysis product of a product derived from the DLS or from the phosphorochloridite;

providing a pre-determined goal for a conversion of phosphorochloridite in the first reaction mixture;

adding the bisaryl compound to the phosphorochloridite in a first serial addition to provide a first reaction mixture, wherein the amount of bisaryl compound added is sufficient to cause the percent conversion of the phosphorochloridite in the first reaction mixture to be equal to or greater than the pre-determined goal for a conversion of the phosphorochloridite in the first reaction mixture;

determining the mole percent of phosphorus present in the first reaction mixture as TLS;

determining the mole percent of phosphorus present in the first reaction mixture as CLS;

determining the percent conversion of the phosphorochloridite in the first reaction mixture;

wherein if in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition includes water;

wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition includes the alcohol having the chemical structure $R^1$-OH or $R^2$-OH;

wherein if in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction product is less than the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture, then second serial addition includes the bisaryl compound, wherein the quantity of the bisaryl compound to add in the second serial addition is determined using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of the bisaryl compound to add in the second serial addition, including:

using at least one selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range in combination with the determined mole percents of TLS and CLS in the first reaction mixture to forecast a maximum percent conversion of phosphorochloridite such that at the forecasted percent conversion in the second reaction mixture the percent of phosphorus present as CLS in the second reaction mixture is less than the pre-determined limit for the percent of phosphorus present as CLS in the final reaction mixture; and

setting a pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to the forecasted maximum percent conversion of the phosphorochloridite;

adding the second serial addition to the first reaction mixture, including a compound selected from the group consisting of the bisaryl compound, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the second reaction mixture, wherein if bisaryl compound is added in the second serial addition then the amount of the bisaryl compound in the second serial addition is sufficient to cause the percent conversion of the phosphorochloridite in the second reaction mixture to be about equal to the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture; and

either

performing third addition steps including

optionally determining a mole percent of phosphorus present in the second reaction mixture as at least one side-product;

optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of water and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition; and

adding the third serial addition to the second reaction mixture to provide the final reaction mixture, wherein the quantities of the one or more compounds added in the third addition are such that the conversion of the phosphorochloridite in the final reaction mixture is about 100%;

or

the final reaction mixture is the second reaction mixture, wherein the quantities of the one or more compounds added in the second addition are such that conversion of the phosphorochloridite in the final reaction mixture is about 100%;

wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; and each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

**[00259]** Embodiment 91 provides the apparatus or method of any one or any combination of Embodiments 1-90 optionally configured such that all elements or options recited are available to use or select from.

## EXEMPLARY EMBODIMENTS

### Mole Ratios During Contacting

**[00260]** In some embodiments, certain mole ratios can be controlled to give optimum selectivity for formation of DLS with concurrent optimal minimization of CLS and TLS formation as well as optimal conversion of the phosphorochloridite. There are various mole ratios that can be controlled, as well as various methods of controlling mole ratios, which can result in optimization of the reaction procedure. The mole ratios described in this section are merely examples of optimization, in some examples controlling these mole ratios can be used alone to optimize the method; other optimization methods are also given outside this section (e.g. that can include at least some analysis of mole ratios) which in various embodiments can be used alone or together with the methods given in this section.

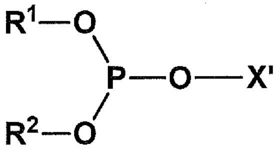
**[00261]** Mole ratio A is defined as the ratio of moles of phosphorochloridite in the reaction mixture to the moles of bisaryl compound fed to the reaction mixture; e.g. moles of phosphorochloridite in the reaction mixture divided by moles of bisaryl compound fed to the reaction mixture. In some embodiments, high selectivities for forming DLS can be obtained by controlling the feeding during a stage of the contacting such that mole ratio A is at least about 2. When mole ratio A is below about 2, the formation of CLS and TLS increase, which decreases the selectivity for DLS. In some embodiments, during a stage of the contacting with high phosphorochloridite conversion, for example between about 90% and about 100%, higher selectivities to the desired diphosphite can also be achieved by controlling the feeding such that mole ratio A is between about 2.1 to about 2.7. The phosphorochloridite conversion is the percent of the total moles of phosphorochloridite added to the reaction mixture that have been converted to other materials.

**[00262]** Mole ratio B is defined as the moles of basic nitrogen atoms from the tertiary organic amine fed to the reaction mixture to moles of phosphorochloridite in the reaction mixture; e.g. moles of basic nitrogen atoms from the tertiary organic amine fed to the reaction mixture divided by moles of phosphorochloridite in the reaction mixture. In some embodiments, high selectivities for formation of DLS can be obtained by controlling the feeding during a stage of the contacting such that mole ratio B is at least about 1. In some embodiments, when mole ratio B is below about 1, the formation of CLS and TLS can increase, decreasing selectivity for DLS formation. In some embodiments, higher selectivities to the desired diphosphite can be achieved by controlling the feeding such that the mole ratio B is between about 1.0 to about 1.5.

**[00263]** Mole ratios A or B can be controlled by calculating or otherwise determining the total moles of phosphorochloridite presently in the reaction mixture and calculating or otherwise determining at least one of the moles of basic nitrogen atoms from the tertiary organic amine fed to the reaction mixture or the moles of bisaryl compound fed to the reaction mixture. Once mole ratios A or B are determined, then the feed rate or quantity added of at least one of the phosphorochloridite, the tertiary organic amine, or the bisaryl compound can be adjusted accordingly. In some embodiments, in the absence of significant water (e.g. < about 300 ppm by weight $H_2O$) entering the reaction mixture with the bisaryl compound, the tertiary organic amine, aromatic hydrocarbon solvent, hydrocarbon solvent, or a combination of these members, these quantities can be calculated or otherwise determined more easily. In some embodiments, determining mole ratios A and B can include withdrawing samples to analyze the liquid reaction mixture, for example by $^{31}P$ NMR, liquid or gas chromatography, mass spectrometry, or any combination thereof.

# CLAIMS

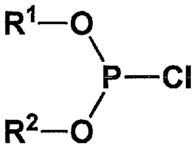
1. A method for producing a phosphorus-containing ligand structure having the following chemical structure



**Structure I'**

comprising:

contacting a phosphorochloridite of the following structure,



**Structure II**

with a compound having the chemical structure X-OH and a tertiary organic amine to provide a final reaction mixture comprising the ligand structure;

wherein the contacting comprises

providing a pre-determined limit for a mole percent of phosphorus present as at least one side-product in the final reaction mixture;

adding the X-OH to the phosphorochloridite in a first serial addition, to provide a first reaction mixture;

determining a mole percent of phosphorus present in the first reaction mixture as the at least one side-product;

using a comparison of the mole percent of phosphorus present in the first reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and an alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a second serial addition;

adding the second serial addition to the first reaction mixture, comprising a compound selected from the group consisting of the X-OH, water, or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide a second reaction mixture; and either

performing third addition steps comprising

optionally determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product;

optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition; and

adding the third serial addition to the second reaction mixture, comprising a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture;

or

the final reaction mixture is the second reaction mixture;

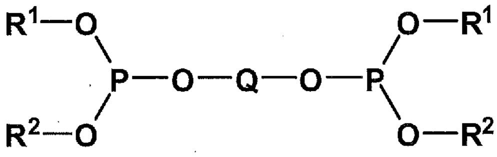
wherein in Structures I' and II, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; $R^1$ and $R^2$ are bridged to one another or unbridged to one another; and each of X and X' are independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, phosphitylbisaryl, phosphitylbisheteroaryl, hydroxybisaryl, hydroxybisheteroaryl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups.

2. The method of claim 1, wherein third addition steps are performed and further comprise:

determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product; and

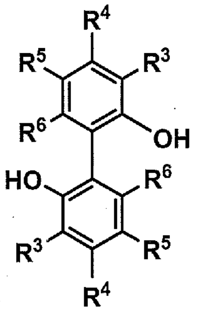
using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition.

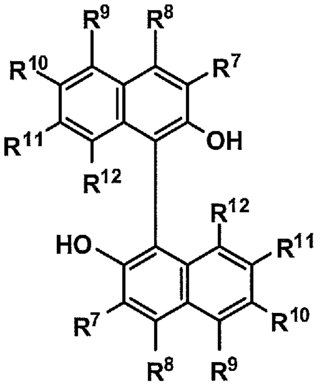
3. The method of claim 1, wherein the ligand structure of Structure I' is a diphosphite ligand structure (DLS) having the chemical structure of Structure I,

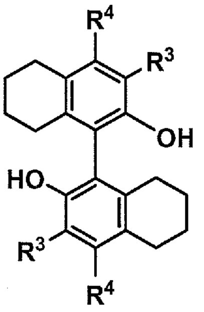


**Structure I**

wherein the X-OH is a bisaryl compound selected from the group consisting of Structure III, Structure IV, and Structure V,



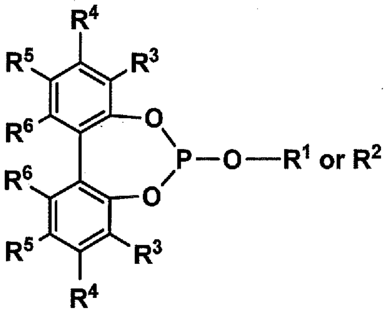




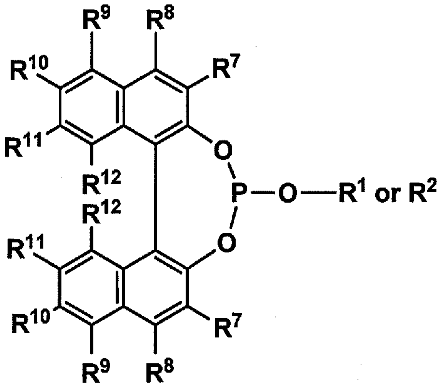
**Structure III** **Structure IV** **Structure V**;

wherein in Structures I-V, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; each of $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ is independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups; and O-Q-O is a divalent species of the bisaryl compound.

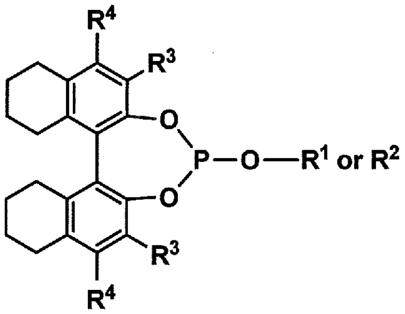
4. The method of claim 1, wherein the at least one side-product comprises a C-phite ligand structure (CLS), having the chemical structure shown below as Structure VI, VII, or VIII,



Structure VI



Structure VII



Structure VIII

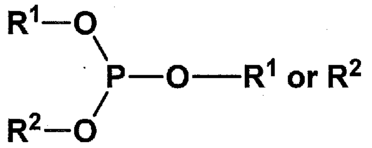
wherein in Structures VI-VIII, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; $R^1$ and $R^2$ are bridged to one another or unbridged to one another; and each of $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ is independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups;

wherein providing a pre-determined limit for the mole percent of phosphorus present as at least one side-product in the final reaction mixture comprises providing a pre-determined limit for a mole percent of phosphorus present as CLS in the final reaction mixture.

5. The method of claim 4, wherein in the final reaction mixture, the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 65%, and the percentage of phosphorus present as the CLS is less than about 5%.

6. The method of claim 4, wherein in the final reaction mixture, the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 70%, and the percentage of phosphorus present as the CLS is less than about 3.5%.

7. The method of claim 1, wherein the at least one side-product comprises a T-phite ligand structure (TLS), having the chemical structure shown below as Structure IX,

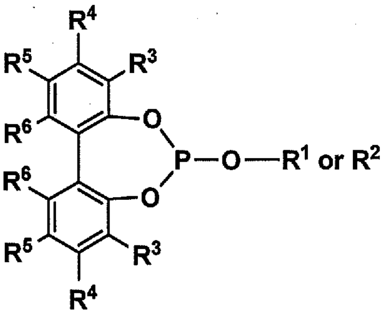


**Structure IX**;

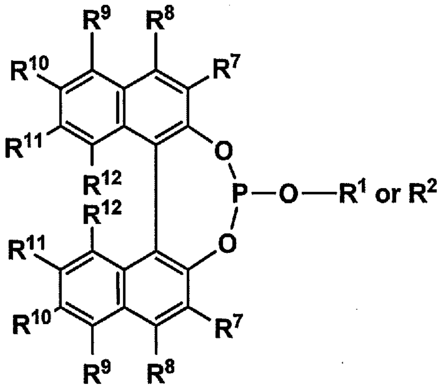
wherein in Structure IX, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; and $R^1$ and $R^2$ are bridged to one another or unbridged to one another;

wherein providing a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture comprises providing a pre-determined limit for a mole percent of phosphorus present as TLS in the final reaction mixture.

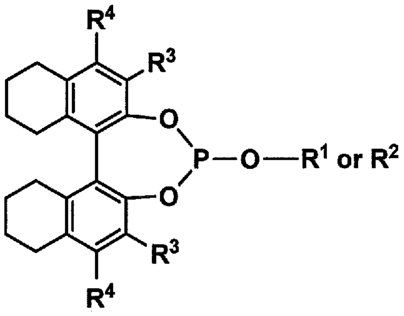
8. The method of claim 1, wherein the at least one side-product comprises a C-phite ligand structure (CLS), having the chemical structure shown below as Structure VI, VII, or VIII,



**Structure VI**

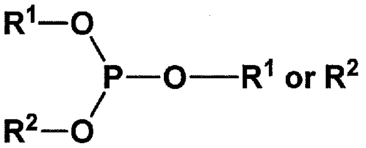


**Structure VII**



**Structure VIII**;

wherein the at least one side-product further comprises a T-phite ligand structure (TLS), having the chemical structure shown below as Structure IX,



**Structure IX**;

wherein in Structures VI-VIII and IX, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; $R^1$ and $R^2$ are bridged to one another or unbridged to one another; and each of $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ is independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups;

wherein providing a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture comprises providing a pre-determined limit for a mole percent of phosphorus present as TLS in the final reaction mixture;

wherein providing a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture comprises providing a pre-determined limit for a mole percent of phosphorus present as CLS in the final reaction mixture.

9. The method of claim 1, wherein the at least one side-product comprises a ligand hydrolysis product (LHP), comprising a product derived by a process comprising

hydrolysis of the phosphorus-containing ligand or of the phosphorochloridite;

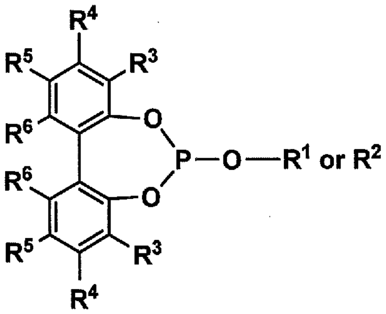
hydrolysis of a product derived from the phosphorus-containing ligand or from the phosphorochloridite; or reaction of the hydrolysis product of the phosphorus-containing ligand or of the phosphorochloridite, or reaction of the hydrolysis product of a product derived from the phosphorus-containing ligand or from the phosphorochloridite;

wherein providing a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture comprises providing a pre-determined limit for a mole percent of phosphorus present as LHP in the final reaction mixture.

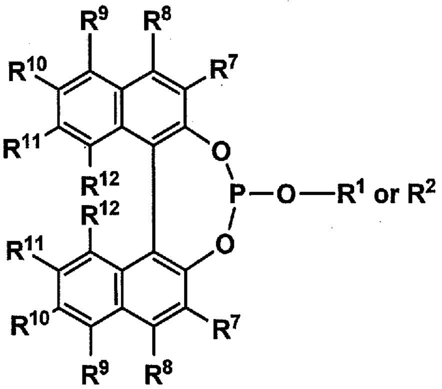
10. The method of claim 9, wherein in the final reaction mixture, the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 65%, and the percentage of phosphorus present as the LHP is less than no more than about 5%.

11. The method of claim 9, wherein in the final reaction mixture, the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 70%, and the percentage of phosphorus present as the LHP is less than no more than about 3.5%.

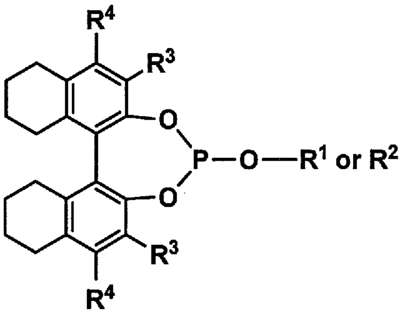
12. The method of claim 1, wherein the at least one side-product comprises a C-phite ligand structure (CLS), having the chemical structure shown below as Structure VI, VII, or VIII,



**Structure VI**

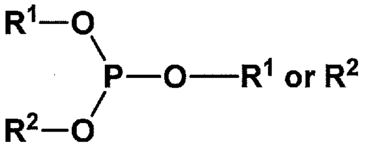


**Structure VII**



**Structure VIII**;

wherein the at least one side-product further comprises a T-phite ligand structure (TLS), having the chemical structure shown below as Structure IX,



**Structure IX**;

wherein in Structures VI-VIII and IX, $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; $R^1$ and $R^2$ are bridged to one another or unbridged to one another; and each of $R^3$, $R^4$, $R^5$, $R^6$, $R^7$, $R^8$, $R^9$, $R^{10}$, $R^{11}$, and $R^{12}$ is independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, aryloxy, heteroaryloxy, alkyloxy, alkoxyalkyl, acetal, carboaryloxy, carboalkoxy, arylcarbonyl, alkylcarbonyl, oxazole, amine, amide, nitrile, mercaptyl, and halogen groups;

wherein providing a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture comprises providing a pre-determined limit for a mole percent of phosphorus present as TLS in the final reaction mixture;

wherein providing a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture comprises providing a pre-determined limit for a mole percent of phosphorus present as CLS in the final reaction mixture;

wherein the at least one side-product further comprises a ligand hydrolysis product (LHP), comprising a product derived by a process comprising

hydrolysis of the phosphorus-containing ligand or of the phosphorochloridite;

hydrolysis of a product derived from the phosphorus-containing ligand or from the phosphorochloridite; or reaction of the hydrolysis product of the phosphorus-containing ligand or of the phosphorochloridite, or reaction of the hydrolysis product of a product derived from the phosphorus-containing ligand or from the phosphorochloridite;

wherein providing a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture comprises providing a pre-determined limit for a mole percent of phosphorus present as LHP in the final reaction mixture.

13. The method of claim 1, wherein the contacting further comprises using the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture to determine an amount of the X-OH to add in the first or second serial addition to cause a mole percent of phosphorus present in the first or second reaction mixtures as the at least one side-product to be less than the pre-determined limit of the mole percent of phosphorus present as the at least one side-product in the final reaction mixture.

14. The method of claim 2, wherein the contacting further comprises using the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture to determine an amount of the X-OH to add in the third serial addition to cause a mole percent of phosphorus present in the final reaction mixture as the at least one side-product to be less than the pre-determined limit of the mole percent of phosphorus present as the at least one side-product in the final reaction mixture.

15. The method of claim 1, wherein the amount of the X-OH added in the second serial addition is less than the amount of the X-OH added in the first serial addition; and wherein the amount of the X-OH added in the third serial addition if performed is equal to or less than the amount of the X-OH added in the second serial addition.

16. The method of claim 1, wherein the amount of the X-OH added in the second or third serial addition is none.

17. The method of claim 1, wherein if the amount of the X-OH added in the second serial addition is none, then the second serial addition comprises at least one of water or the alcohol

having the chemical structure $R^1$-OH or $R^2$-OH; and wherein if the amount of the X-OH added in the third serial addition is none, then the third serial addition if performed comprises at least one of water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

18. The method of claim 4, wherein using a comparison of the mole percent of phosphorus present in the first or second reaction mixture as the CLS to the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture to determine the amount of a compound to add in the second serial addition or the third serial addition if performed comprises adding an amount of a compound in the second or third addition selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH sufficient to cause the mole percent of phosphorus in the second or final reaction mixture present as the CLS to be equal to or below the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture.

19. The method of claim 18, wherein if the mole percent of phosphorus present in the first reaction mixture as the CLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, then the second serial addition comprises water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and wherein if the mole percent of phosphorus present in the second reaction mixture as the CLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, then the third serial addition if performed comprises water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

20. The method of claim 18, wherein if the mole percent of phosphorus present in the first reaction mixture as the CLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, then the second serial addition does not include the X-OH; and wherein if the mole percent of phosphorus present in the second reaction mixture as the CLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, then the third addition if performed does not include the X-OH.

21. The method of claim 7, wherein using a comparison of the mole percent of phosphorus present in the first or second reaction mixture as the TLS to the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture to determine the amount of a compound to add in the second or third serial addition comprises adding an amount of a compound in the second or third addition selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH sufficient to cause the mole percent of phosphorus in the second or final reaction mixture present as the TLS to be equal to or below the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture.

22. The method of 21, wherein if the mole percent of phosphorus present in the first reaction mixture as the TLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the second serial addition comprises water; and wherein if the mole percent of phosphorus present in the second reaction mixture as the TLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the third serial addition if performed comprises water.

23. The method of 21, wherein if the mole percent of phosphorus present in the first reaction mixture as TLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the second serial addition does not include the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and wherein if the mole percent of phosphorus present in the second reaction mixture as TLS is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the third serial addition if performed does not include the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

24. The method of claim 9, wherein using a comparison of the mole percent of phosphorus present in the first or second reaction mixture as the LHP to the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture to determine the amount of a compound to add in the second or third serial addition comprises adding an amount

of a compound in the second or third addition selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH sufficient to cause the mole percent of phosphorus in the second or final reaction mixture present as the LHP to be equal to or below the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture.

25. The method of 24, wherein if the mole percent of phosphorus present in the first reaction mixture as LHP is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture, then the second serial addition comprises the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and wherein if the mole percent of phosphorus present in the second reaction mixture as LHP is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture, then the third serial addition if performed comprises the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

26. The method of 24, wherein if the mole percent of phosphorus present in the first reaction mixture as LHP is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture, then the second serial addition does not include water; and wherein if the mole percent of phosphorus present in the second reaction mixture as LHP is equal to or greater than the pre-determined limit for the mole percent of phosphorus present as the LHP in the final reaction mixture, then the third serial addition if performed does not include water.

27. The method of claim 8, wherein if in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition comprises water; and wherein if in the second reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the third serial addition if performed comprises water.

28. The method of claim 8, wherein if in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition does not include the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and wherein if in the second reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then if performed the third serial addition does not include the X-OH or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

29. The method of claim 1, wherein the contacting further comprises:

providing a pre-determined goal for a conversion of phosphorochloridite in the second reaction mixture;

after adding the first serial addition, determining the percent conversion of the phosphorochloridite in the first reaction mixture; and

before adding the second serial addition, using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of the X-OH to add in the second serial addition.

30. The method of claim 8, wherein the contacting further comprises:

providing a pre-determined goal for a conversion of phosphorochloridite in the second reaction mixture;

after adding the first serial addition, determining the percent conversion of the phosphorochloridite in the first reaction mixture; and

before adding the second serial addition, using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of the X-OH to add in the second serial addition.

31. The method of claim 30, wherein if in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor as the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or as the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction mixture is less than the pre-determined goal for the conversion of phosphorochloridite in the final reaction mixture, then the amount of the X-OH to add in the second serial addition is sufficient to make the percent conversion of the phosphorochloridite in the second reaction mixture equal to or above the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture.

32. The method of claim 30, wherein if in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor as the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or as the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction mixture is less than the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture, then the second serial addition does not include water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

33. The method of claim 1 or 29, wherein if percent conversion of the phosphorochloridite in the second reaction mixture is less than about 100%, then further comprising adding the third serial addition to the second reaction mixture, wherein the third serial addition comprises a sufficient quantity of water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH such that following the third serial addition the phosphorochloridite conversion in the final reaction mixture is about 100%.

34. The method of claim 7, further comprising determining the percent conversion of the phosphorochloridite in the second reaction mixture and determining the mole percent of phosphorus present as TLS in the second reaction mixture, wherein if percent conversion of the phosphorochloridite in the second reaction mixture is less than about 100%, and if in the second reaction mixture the mole percent of phosphorus present as TLS is less than the pre-determined limit for the mole percent of phosphorus present as TLS in the final reaction mixture, then

further comprising adding the third serial addition to the second reaction mixture, wherein the third serial addition comprises a sufficient quantity of the alcohol having the chemical structure $R^1$-OH or $R^2$-OH such that following the third serial addition the conversion of the phosphorochloridite in the final reaction mixture is about 100%.

35. The method of claim 9, wherein if percent conversion of the phosphorochloridite in the second reaction mixture is less than about 100%, and if in the second reaction mixture the mole percent of phosphorus present as LHP is less than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then further comprising adding a third serial addition to the second reaction mixture, wherein the third serial addition comprises a sufficient quantity of water such that following the third serial addition the conversion of the phosphorochloridite in the final reaction mixture is about 100%.

36. The method of claim 35, wherein following the third serial addition, in the final reaction mixture the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 65% and the percentage of phosphorus present as the LHP is less than about 5%.

37. The method of claim 35, wherein following the third serial addition, in the final reaction mixture the percentage of phosphorus present as the phosphorus-containing ligand structure is greater than or equal to about 70%, and the percentage of phosphorus present as the LHP is less than about 3.5%.

38. The method of claim 1, wherein the contacting further comprises:

providing a pre-determined goal for a conversion of phosphorochloridite in the first reaction mixture;

before adding the first serial addition, using the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture to determine the amount of the X-OH to add in the first serial addition, such that the conversion of phosphorochloridite in the first reaction mixture is at or above the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture.

39. The method of claim 9, wherein the contacting further comprises:

providing a pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture;

after adding the first serial addition, determining the mole percent of phosphorus present as LHP in the first reaction mixture; and

before adding the second serial addition, using a comparison of the mole percent of phosphorus present as LHP in the first reaction mixture to the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture to determine the composition of the second serial addition.

40. The method of claim 12, wherein the contacting further comprises:

providing a pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture;

after adding the first serial addition, determining the mole percent of phosphorus present as LHP in the first reaction mixture; and

before adding the second serial addition, using a comparison of the mole percent of phosphorus present as LHP in the first reaction mixture to the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture to determine the composition of the second serial addition.

41. The method of claim 40, wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition comprises the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

42. The method of claim 40, wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition does not include the X-OH or water.

43. The method of claim 8, wherein the contacting further comprises:

providing a pre-determined goal for a conversion of phosphorochloridite in the second reaction mixture; and

after adding the first serial addition,

determining the percent conversion of the phosphorochloridite in the first reaction mixture; and

wherein if in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition comprises water;

wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the second serial addition comprises water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and

wherein if in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor as the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction product is less than the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture, then the second serial comprises a sufficient amount of the X-OH such that the percent conversion of the phosphorochloridite in the second reaction mixture is equal to or above the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture.

44. The method of claim 43, wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, then the second serial addition comprises the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

45. The method of claim 12, wherein the contacting further comprises:

providing a pre-determined goal for a conversion of phosphorochloridite in the second reaction mixture; and

after adding the first serial addition,

determining the percent conversion of the phosphorochloridite in the first reaction mixture; and

determining the mole percent of phosphorus present as LHP in the first reaction mixture;

wherein if in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition comprises water;

wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition comprises the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and wherein if in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction product is less than the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture, then second serial addition comprises X-OH in sufficient quantity such that the percent conversion of the phosphorochloridite in the second reaction mixture is equal to or above the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture.

46. The method of claim 45, wherein contacting further comprises:

wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is not equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition comprises water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH; and

wherein if in the first reaction mixture the mole percent of phosphorus present as the TLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the CLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is not equal or to greater than the pre-determined limit for LHP content in the final reaction mixture, then the second addition comprises water.

47. The method of claim 45, wherein contacting further comprises:

wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the

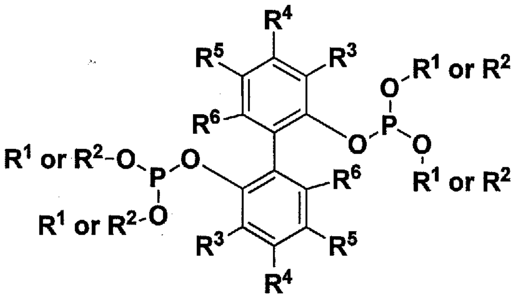
CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is not equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition does not include the X-OH; and

wherein if in the first reaction mixture the mole percent of phosphorus present as the TLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the CLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is not equal or to greater than the pre-determined limit for LHP content in the final reaction mixture, then the second addition does not include water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH.

48. The method of claim 1, wherein the first reaction mixture has a stoichiometric excess of phosphorochloridite.

49. The method of claim 1, wherein the contacting is carried out in the presence of a stoichiometric excess of tertiary organic amine.

50. The method of claim 1, wherein the phosphorus-containing ligand has the following chemical structure:

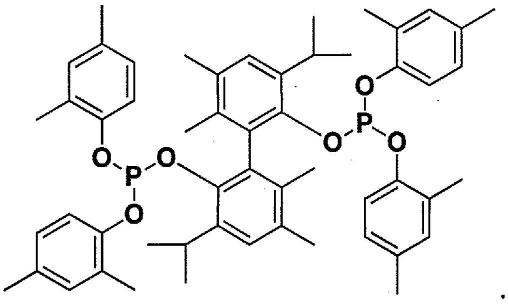


wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

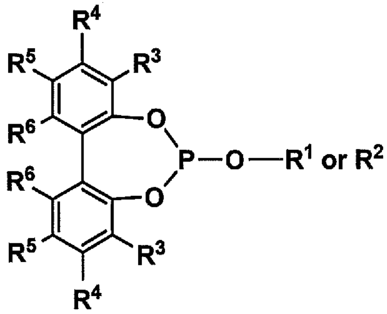
51. The method of claim 1, wherein $R^2 = R^1$, wherein $R^1$ is a monovalent xylene group.

52. The method of claim 1, wherein $R^2 = R^1$, wherein $R^1$ is a monovalent 2,4-xylene group

53. The method of claim 1, wherein the phosphorus-containing ligand has the following chemical structure:

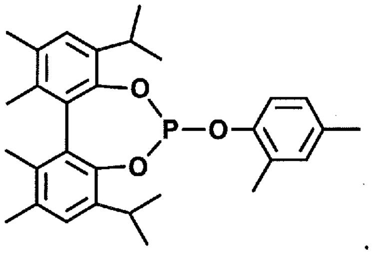


54. The method of claim 4, wherein the CLS has the following chemical structure:



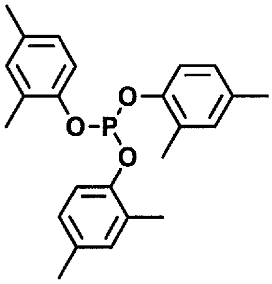
wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

55. The method of claim 4, wherein the CLS has the following chemical structure:



56. The method of claim 7, wherein the TLS has the chemical structure $P(OR^1)_3$, wherein $R^1$ is a substituted or unsubstituted aryl group.

57. The method of claim 7, wherein the TLS has the following chemical structure:



58. The method of claim 1, wherein the tertiary organic amine comprises a trialkylamine.

59. The method of claim 1, wherein the tertiary organic amine comprises triethylamine.

60. The method of claim 4, wherein the pre-determined limit for the mole percent phosphorus present as the CLS in the final reaction mixture is less than or equal to about 5%.

61. The method of claim 4, wherein the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture is less than or equal to about 3%.

62. The method of any one of claims 30, 43, or 45, wherein using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of the X-OH to add in the second serial addition comprises:

using at least one selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range to forecast a maximum percent conversion of phosphorochloridite such that at the forecasted percent conversion in the second reaction mixture the percent of phosphorus present as CLS in the second reaction mixture is less than the pre-determined limit for the percent of phosphorus present as CLS in the final reaction mixture;

setting the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to the forecasted maximum percent conversion of the phosphorochloridite; and

adding an amount of the X-OH in the second serial addition sufficient to cause the percent conversion of the phosphorochloridite in the second reaction mixture to be about equal to the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture.

63. The method of claim 62, wherein the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range comprises a molar selectivity ratio of CLS to phosphorus-containing ligand of about 1:6 for conversions up to about 98%.

64. The method of claim 62, wherein the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range comprises a molar selectivity ratio of CLS to phosphorus-containing ligand of about 1:1 for conversions of between about 98% and about 100%.

65. The method of claim 7, wherein the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture is less than or equal to about 30%.

66. The method of claim 7, wherein the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture is less than or equal to about 22%.

67. The method of any one of claims 30, 43, or 45, wherein using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined

goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of the X-OH to add in the second serial addition comprises:

using at least one selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and TLS at a given conversion range to forecast a maximum percent conversion of phosphorochloridite such that at the forecasted percent conversion in the second reaction mixture the percent of phosphorus present as TLS in the second reaction mixture is less than the pre-determined limit for the percent of phosphorus present as TLS in the final reaction mixture;

setting the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to the forecasted maximum percent conversion of the phosphorochloridite; and

adding an amount of the X-OH in the second serial addition sufficient to cause the percent conversion of the phosphorochloridite in the second reaction mixture to be about equal to the pre-determined goal for the percent conversion of the phosphorochloridite in the second reaction mixture.

68. The method of claim 67, wherein the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range comprises a molar selectivity ratio of CLS to phosphorus-containing ligand of about 1:6 for conversions up to about 98%.

69. The method of claim 67, wherein the selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range comprises a molar selectivity ratio of CLS to phosphorus-containing ligand of about 1:1 for conversions of between about 98% and about 100%.

70. The method of any one of claims 29, 30, 43, or 45, wherein the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture is about 95% to about 100%.

71. The method of any one of claims 29, 30, 43, or 45, wherein the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture is about 96% to about 99%.

72. The method of claim 38, wherein the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture is about 85% to about 95%.

73. The method of claim 38, wherein the pre-determined goal for the conversion of phosphorochloridite in the first reaction mixture is about 90%.

74. The method of any one of claims 39, 40, or 45, wherein the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture is about 5%.

75. The method of any one of claims 39, 40, or 45, wherein the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture is about 3%.

76. The method of claim 1, wherein the contacting is carried out by at least one step selected from the group consisting of

(i) feeding the X-OH to a mixture of the phosphorochloridite and the tertiary organic amine;

(ii) feeding the X-OH and the tertiary organic amine separately to the phosphorochloridite; or

(iii) feeding the X-OH and the tertiary organic amine as a mixture to the phosphorochloridite.

77. The method of claim 1 wherein the reaction mixture further comprises at least one aromatic hydrocarbon solvent.

78. The method of claim 77 wherein the aromatic solvent comprises toluene.

79. The method of claim 77 further comprising feeding the X-OH to the phosphorochloridite as a solution comprising the X-OH and the hydrocarbon solvent.

80. The phosphorus-containing ligand of Structure I made by the method of claim 1.

81. The method of claim 1, wherein

the first serial addition comprises the X-OH in sufficient quantity such that the conversion of the phosphorochloridite in the first reaction mixture is about 85% to about 95%; and

the second serial addition comprises a smaller amount of the X-OH than the amount of the X-OH added in the first serial addition.

82. The method of claim 1, wherein

the first serial addition comprises X-OH in sufficient quantity such that the conversion of the phosphorochloridite in the first reaction mixture is about 85% to about 90%; and

the second serial addition comprises the alcohol having the chemical structure $R^1$-OH or $R^2$-OH in sufficient quantity such that in the second reaction mixture phosphorochloridite conversion is about 100%.

83. The method of claim 1, wherein

the first serial addition comprises the X-OH in sufficient quantity such that the conversion of the phosphorochloridite in the first reaction mixture is about 85% to about 95%; and

after the second serial addition, the conversion of the phosphorochloridite in the second reaction mixture is about 95% to about 99%;

the third serial addition comprises water or the alcohol having the chemical structure $R^1$-OH or $R^2$-OH in sufficient quantity such that the conversion of the phosphorochloridite in the final reaction mixture is about 100%.

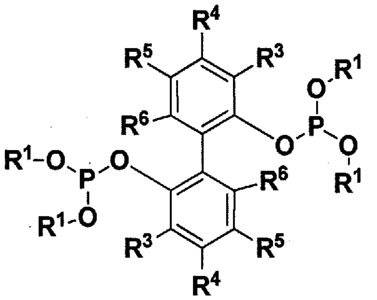
84. The method of claim 1, wherein the method gives a final reaction mixture that is a first final reaction mixture, wherein the method is repeated to give a second final reaction mixture, wherein the yield of the phosphorus-containing ligand in the first final reaction mixture is within 5% of the yield of the phosphorus-containing ligand in the second final reaction mixture.

85. The method of claim 4, wherein the method gives a final reaction mixture that is a first final reaction mixture, wherein the method is repeated to give a second final reaction mixture,

wherein the percentage of phosphorus in the first final reaction mixture present as the phosphorus-containing ligand, TLS, and CLS, is each within 5% of the percentage of phosphorus in the second final reaction mixture present as the phosphorus-containing ligand, TLS, and CLS, respectively.

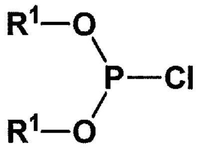
86. The method of claim 4, wherein the method gives a final reaction mixture that is a first final reaction mixture, wherein the method is repeated to give a second final reaction mixture, wherein the percentage of phosphorus in the first final reaction mixture present as CLS is within 5% of the percentage of phosphorus in the second final reaction mixture present as the CLS.

87. A method for producing a diphosphite ligand structure (DLS) having the following structure,

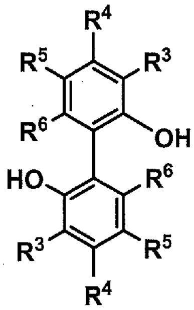


comprising:

contacting a phosphorochloridite having the following structure,



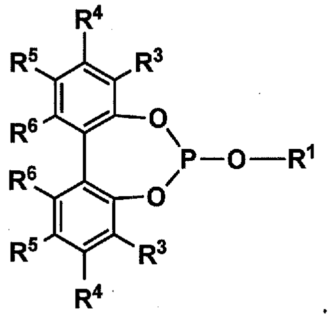
with a bisaryl compound having the following structure,



and a tertiary organic amine to provide a final reaction mixture comprising the diphosphite;

wherein the contacting comprises

providing a pre-determined limit for the mole percent of phosphorus present as C-phite ligand structure (CLS), having the chemical structure shown below, in the final reaction mixture



adding the bisaryl compound to the phosphorochloridite in a first serial addition such that the moles of phosphorochloridite added in the first addition is greater than the number of moles of the bisaryl compound added in the first addition, to provide a first reaction mixture;

determining the mole percent of phosphorus present in the first reaction mixture as CLS;

using a comparison of the mole percent of phosphorus present in the first reaction mixture as CLS to the pre-determined limit for the mole percent of phosphorus present as CLS to determine an amount of a compound selected from the group consisting of at least one of the bisaryl compound, water, and an alcohol having the chemical structure $R^1$-OH, to add in a second serial addition such that the mole percent of phosphorus present as CLS in a second reaction mixture is less than or equal to the pre-determined limit for the mole percent of phosphorus present as CLS in the final reaction mixture;

adding the second serial addition to the first reaction mixture, comprising a compound selected from the group consisting of the bisaryl compound, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the second reaction mixture; and

either

performing third addition steps comprising

optionally determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product;

optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition; and

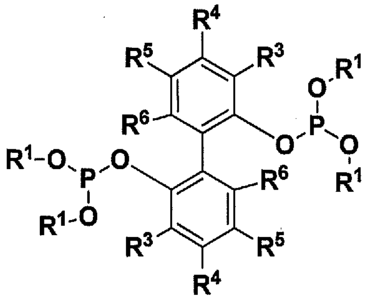
adding the third serial addition to the second reaction mixture, comprising a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture;

or

the final reaction mixture is the second reaction mixture;

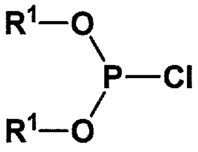
wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

88. A method for producing a diphosphite ligand structure (DLS) having the following structure,

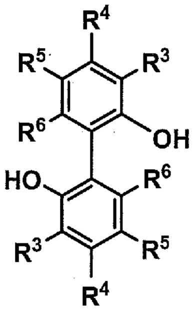


comprising:

contacting a phosphorochloridite having the following structure,



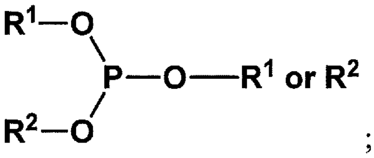
with a bisaryl compound having the following structure,



and a tertiary organic amine to provide a final reaction mixture comprising the diphosphite;

wherein the contacting comprises

providing a pre-determined limit for the mole percent of phosphorus present as T-phite ligand structure (TLS), having the chemical structure shown below, in the final reaction mixture



;

adding the bisaryl compound to the phosphorochloridite in a first serial addition such that the moles of phosphorochloridite added in the first addition is greater than the number of moles of biaryl added in the first addition, to provide a first reaction mixture;

determining the mole percent of phosphorus present in the first reaction mixture as TLS;

using a comparison of the mole percent of phosphorus present in the first reaction mixture as TLS to the pre-determined limit for the mole percent of phosphorus present as TLS to determine an amount of a compound selected from the group consisting of the bisaryl compound, water, and an alcohol having the chemical structure $R^1$-OH, to add in a second serial addition such that the mole percent of phosphorus present as TLS in a second reaction mixture is less than or equal to the pre-determined limit for the mole percent of phosphorus present as TLS in the final reaction mixture;

adding the second serial addition to the first reaction mixture, comprising a compound selected from the group consisting of the bisaryl compound, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the second reaction mixture; and

either

performing third addition steps comprising optionally determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product;

optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition; and

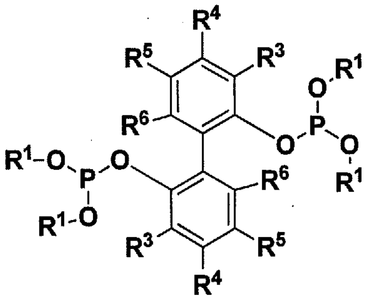
adding the third serial addition to the second reaction mixture, comprising a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture;

or

the final reaction mixture is the second reaction mixture;

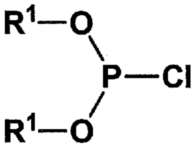
wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; and each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

89. A method for producing a diphosphite ligand structure (DLS) having the following structure,

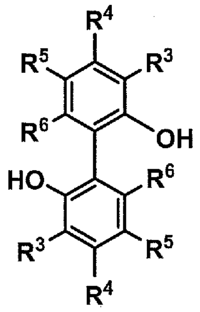


comprising:

contacting a phosphorochloridite having the following structure,



with a bisaryl compound having the following structure,



and a tertiary organic amine to provide a final reaction mixture comprising the diphosphite;

wherein the contacting comprises

providing a pre-determined limit for the mole percent of phosphorus present as a ligand hydrolysis product (LHP) in the final reaction mixture, comprising a product derived by a process comprising

hydrolysis of the DLS or of the phosphorochloridite;

hydrolysis of a product derived from the DLS or from the phosphorochloridite; or

reaction of the hydrolysis product of the DLS or of the phosphorochloridite, or reaction of the hydrolysis product of a product derived from the DLS or from the phosphorochloridite;

adding the bisaryl compound to the phosphorochloridite in a first serial addition such that the moles of phosphorochloridite added in the first addition is greater than the number of moles of biaryl added in the first addition, to provide a first reaction mixture;

determining the mole percent of phosphorus present in the first reaction mixture as LHP;

using a comparison of the mole percent of phosphorus present in the first reaction mixture as LHP to the pre-determined limit for the mole percent of phosphorus present as LHP to determine an amount of a compound selected from the group consisting of the bisaryl compound, water, and an alcohol having the chemical structure $R^1$-OH, to add in a second serial addition such that the mole percent of phosphorus present as LHP in a second reaction mixture is less than or equal to the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture;

adding the second serial addition to the first reaction mixture, comprising a compound selected from the group consisting of the bisaryl compound, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the second reaction mixture; and

either

performing third addition steps comprising

optionally determining a mole percent of phosphorus present in the second reaction mixture as the at least one side-product;

optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to the pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition; and

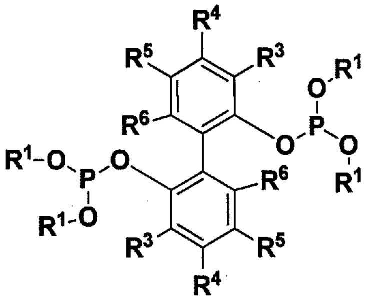
adding the third serial addition to the second reaction mixture, comprising a compound selected from the group consisting of the X-OH, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the final reaction mixture;

or

the final reaction mixture is the second reaction mixture;

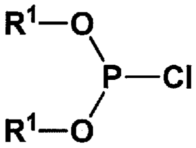
wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; and each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

90. A method for producing a diphosphite ligand structure (DLS) having the following structure,

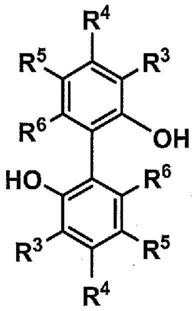


comprising:

contacting a phosphorochloridite having the following structure,



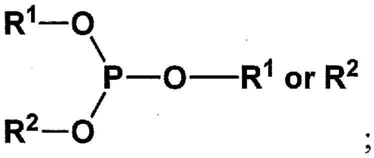
with a bisaryl compound having the following structure,



and a tertiary organic amine to provide a final reaction mixture comprising the diphosphite;

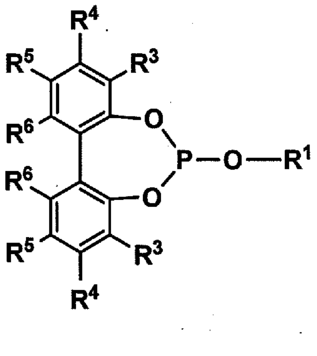
wherein the contacting comprises

providing a pre-determined limit for the mole percent of phosphorus present as T-phite ligand structure (TLS), having the chemical structure shown below, in the final reaction mixture



;

providing a pre-determined limit for the mole percent of phosphorus present as C-phite ligand structure (CLS), having the chemical structure shown below, in the final reaction mixture



providing a pre-determined limit for the mole percent of phosphorus present as a ligand hydrolysis product (LHP) in the final reaction mixture, comprising a product derived by a process comprising

hydrolysis of the DLS or of the phosphorochloridite;

hydrolysis of a product derived from the DLS or from the phosphorochloridite; or

reaction of the hydrolysis product of the DLS or of the phosphorochloridite, or reaction of the hydrolysis product of a product derived from the DLS or from the phosphorochloridite;

providing a pre-determined goal for a conversion of phosphorochloridite in the first reaction mixture;

adding the bisaryl compound to the phosphorochloridite in a first serial addition to provide a first reaction mixture, wherein the amount of bisaryl compound added is sufficient to cause the percent conversion of the phosphorochloridite in the first reaction mixture to be equal to or greater than the pre-determined goal for a conversion of the phosphorochloridite in the first reaction mixture;

determining the mole percent of phosphorus present in the first reaction mixture as TLS;

determining the mole percent of phosphorus present in the first reaction mixture as CLS;

determining the percent conversion of the phosphorochloridite in the first reaction mixture;

wherein if in the first reaction mixture both the mole percents of phosphorus present as the CLS and the TLS are equal to or greater than the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, then the second serial addition comprises water;

wherein if in the first reaction mixture the mole percent of phosphorus present as the CLS is equal to or above the pre-determined limit for the mole percent of phosphorus present as the CLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as the TLS is not equal to or above the pre-determined limit for the mole percent of phosphorus present as the TLS in the final reaction mixture, and in the first reaction mixture the mole percent of phosphorus present as LHP is equal or to greater than the pre-determined limit for the mole percent of phosphorus present as LHP in the final reaction mixture, then the second serial addition comprises the alcohol having the chemical structure $R^1$-OH or $R^2$-OH;

wherein if in the first reaction mixture neither the mole percent of phosphorus present as the CLS nor the TLS is equal to or above the respective pre-determined limits for the mole percents of phosphorus present as the CLS or the TLS in the final reaction mixture, and the conversion of phosphorochloridite in the first reaction product is less than the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture, then second serial addition comprises the bisaryl compound, wherein the quantity of the bisaryl compound to add in the second serial addition is determined using a comparison of the percent conversion of the phosphorochloridite in the first reaction mixture to the pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to determine the amount of the bisaryl compound to add in the second serial addition, comprising:

using at least one selectivity ratio of the phosphorochloridite to the phosphorus-containing ligand and CLS at a given conversion range in combination with the determined mole percents of TLS and CLS in the first reaction mixture to forecast a maximum percent conversion of phosphorochloridite such that at the forecasted percent conversion in the second reaction mixture the percent of phosphorus present as CLS in the second reaction mixture is less than the pre-determined limit for the percent of phosphorus present as CLS in the final reaction mixture; and

setting a pre-determined goal for the conversion of phosphorochloridite in the second reaction mixture to the forecasted maximum percent conversion of the phosphorochloridite;

adding the second serial addition to the first reaction mixture, comprising a compound selected from the group consisting of the bisaryl compound, water, and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to provide the second reaction mixture, wherein if bisaryl compound is added in the second serial addition then the amount of the bisaryl compound in the second serial addition is sufficient to cause the percent conversion of the phosphorochloridite in the second reaction mixture to be about equal to the pre-determined goal for the conversion of the phosphorochloridite in the second reaction mixture; and either

performing third addition steps comprising

optionally determining a mole percent of phosphorus present in the second reaction mixture as at least one side-product;

optionally using a comparison of the mole percent of phosphorus present in the second reaction mixture as the at least one side-product to a pre-determined limit for the mole percent of phosphorus present as the at least one side-product in the final reaction mixture, to determine an amount of a compound selected from the group consisting of water and the alcohol having the chemical structure $R^1$-OH or $R^2$-OH, to add in a third serial addition; and

adding the third serial addition to the second reaction mixture to provide the final reaction mixture, wherein the quantities of the one or more compounds added in the third addition are such that the conversion of the phosphorochloridite in the final reaction mixture is about 100%;

or

the final reaction mixture is the second reaction mixture, wherein the quantities of the one or more compounds added in the second addition are such that conversion of the phosphorochloridite in the final reaction mixture is about 100%;

wherein $R^1$ and $R^2$ are the same or different, substituted or unsubstituted, monovalent aryl groups; and each of $R^3$, $R^4$, $R^5$, $R^6$ is independently selected from the group consisting of hydrogen and $C_{1-10}$ alkyl.

# INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2012/002472

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07F9/145 C07F9/146 C07F9/6574
ADD.

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)
C07F

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)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | WO 2010/123747 A1 (INVISTA TECH SARL [CH]; RITTER JOACHIM C [US]; VOS THOMAS E [US]) 28 October 2010 (2010-10-28) | 1-90 |
| Y | paragraph [0074]; example 14<br>page 26, paragraph 0076 - page 27<br>page 34; compounds Ib, VIIb<br>Reaction product resulting from reaction is identical to that of claim 53 :;<br>page 44, paragraph 0122<br>-----<br>-/-- | 1-79,<br>81-90 |

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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"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

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"&" document member of the same patent family

Date of the actual completion of the international search
8 March 2013

Date of mailing of the international search report
15/03/2013

Name and mailing address of the ISA/
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer
Lange, Tim

## INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2012/002472

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X<br>Y | WO 2008/008930 A2 (INVISTA TECH SARL [US]; FOO THOMAS [US]; GARNER JAMES MICHAEL [US]; OZ) 17 January 2008 (2008-01-17)<br>first two compounds on top of page:;<br>page 21<br>Ligand B;<br>page 27<br>Method of producing a phosphorous-containing organodiphosphite structure of Markush formula (I) by reacting bis-(2,4-dimethylphenoxy)chlorophospite with 3,3'-diisopropyl-5,5',6,6'-tetramethyl-2,2'-bisphenol in the presence of an organic base;<br>page 20, line 28 - line 31<br>----- | 80<br>1-79, 81-90 |
| X<br>Y | WO 2007/109005 A2 (INVISTA TECH SARL [US]; RITTER JOACHIM C [US])<br>27 September 2007 (2007-09-27)<br>page 10; compounds 1,3,7<br>Conversion of bis-(2,4-dimethyl-phenoxy)chlorophosphite 1 to bidentate triorganophosphite 3;<br>page 14; example b<br>----- | 80<br>1-79, 81-90 |

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2012/002472

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
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| | | US 2010076212 A1 | 25-03-2010 |
| | | WO 2007109005 A2 | 27-09-2007 |

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(71)申请人 因温斯特技术公司
地址 瑞士圣加伦

(72)发明人 斯图尔特·福赛思
约翰·阿瑟·特纳 基思·惠斯顿
托马斯·E·沃斯

(74)专利代理机构 中科专利商标代理有限责任公司 11021
代理人 王铁军

(51)Int.Cl.
*C07F 9/145*(2006.01)
*C07F 9/146*(2006.01)
*C07F 9/6574*(2006.01)

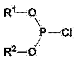
权利要求书24页 说明书73页

(54) 发明名称

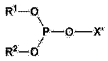
特征在于测量副产物水平以确定进一步添加的由氯代亚磷酸酯制备有机二亚磷酸酯的方法

(57) 摘要

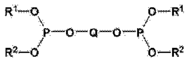
本发明要求保护用于制备含磷配体，优选二亚磷酸酯配体结构(DLS)如结构 I 的方法。所述方法包括使氯代亚磷酸酯（结构 II）与具有结构 X-OH 的化合物（可以为联芳化合物）和有机叔胺接触以提供结构 I′和优选的实施方案结构 I。



结构 II

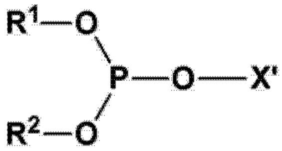


结构 I'



结构 I

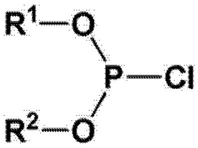
1. 一种用于制备具有以下化学结构的含磷配体结构的方法，



结构 I'

所述方法包括：

使以下结构的氯代亚磷酸酯，



结构 II

与具有化学结构 X-OH 的化合物和有机叔胺接触，以提供包含所述配体结构的最终反应混合物；

其中所述接触包括：

为所述最终反应混合物中作为至少一种副产物存在的磷的摩尔百分比规定预定极限值；

在第一连续添加中将所述 X-OH 添加至所述氯代亚磷酸酯中，以提供第一反应混合物；

确定作为所述至少一种副产物存在于所述第一反应混合物中的磷的摩尔百分比；

利用作为所述至少一种副产物存在于所述第一反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第二连续添加中添加的选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量；

向所述第一反应混合物添加第二连续添加物，包括选自由所述 X-OH、水、或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供第二反应混合物；以及

或者

进行第三添加步骤，所述第三添加步骤包括

任选地确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比；

任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述 X-OH、水、和所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量；以及

向所述第二反应混合物添加第三连续添加物，包括选自由所述 X-OH、水、和所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供所述最终反应混合物；

或者

所述最终反应混合物是所述第二反应混合物；

其中在结构 I'和 II 中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^1$ 和 $R^2$ 彼

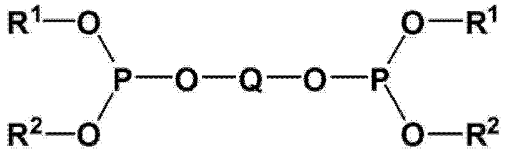
此桥接或彼此不桥接；并且 X 和 X’ 中的每一个独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、亚磷酸酯基联芳基、亚磷酸酯基联杂芳基、羟基联芳基、羟基联杂芳基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团。

2. 根据权利要求 1 所述的方法，其中进行第三添加步骤并且所述第三添加步骤还包括：

确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比；以及

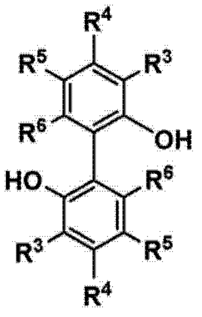
利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述 X-OH、水、和所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量。

3. 根据权利要求 1 所述的方法，其中所述结构 I’ 的配体结构是具有结构 I 的化学结构的二亚磷酸酯配体结构（DLS），

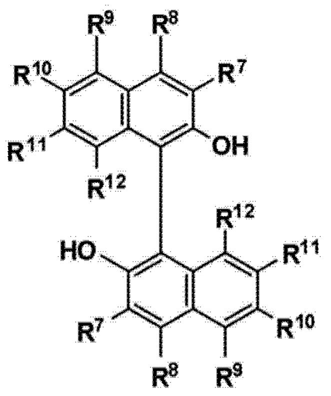


**结构 I**

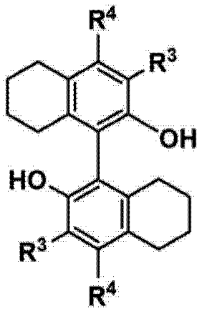
其中所述 X-OH 是选自由结构 III、结构 IV 和结构 V 组成的组的联芳化合物，



**结构 III**



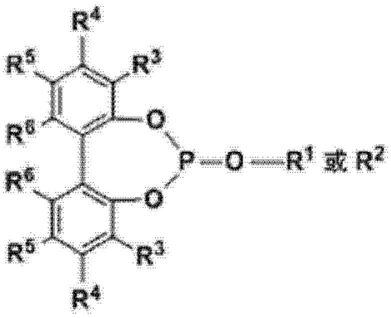
**结构 IV**



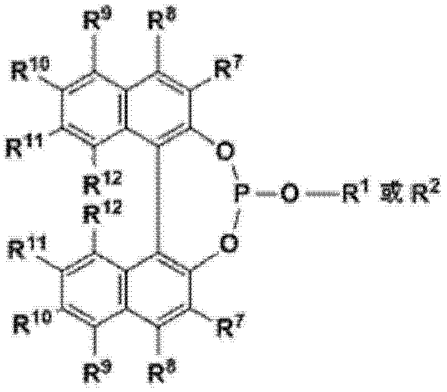
**结构 V；**

其中在结构 I-V 中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和 $R^{12}$ 中的每一个独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团；并且 O-Q-O 是所述联芳化合物的二价物种。

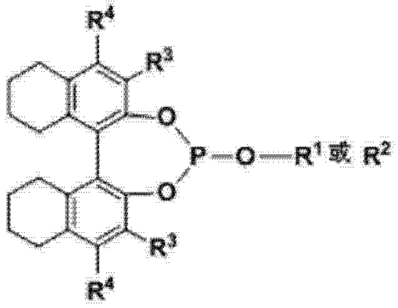
4. 根据权利要求 1 所述的方法，其中所述至少一种副产物包含 C-phite 配体结构（CLS），该 C-phite 配体结构具有如下显示为结构 VI、VII、或 VIII 的化学结构：



**结构 VI**



**结构 VII**



**结构 VIII**

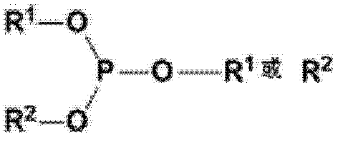
其中在结构 VI-VIII 中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^1$ 和 $R^2$ 彼此桥接或彼此不桥接；并且 $R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和 $R^{12}$ 中的每一个独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团；

其中为所述最终反应混合物中作为至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为 CLS 存在的磷的摩尔百分比规定预定极限值。

5. 根据权利要求 4 所述的方法，其中在所述最终反应混合物中，作为所述含磷配体结构存在的磷的百分比大于或等于约 65%，并且作为所述 CLS 存在的磷的百分比小于约 5%。

6. 根据权利要求 4 所述的方法，其中在所述最终反应混合物中，作为所述含磷配体结构存在的磷的百分比大于或等于约 70%，并且作为所述 CLS 存在的磷的百分比小于约 3.5%。

7. 根据权利要求 1 所述的方法，其中所述至少一种副产物包含 T-phite 配体结构 (TLS)，该 T-phite 配体结构具有如下显示为结构 IX 的化学结构：

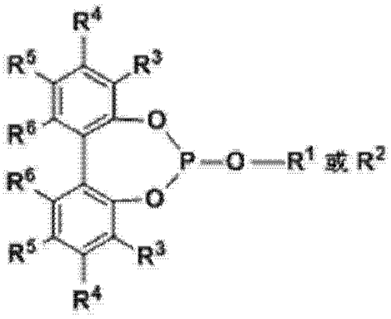


**结构 IX；**

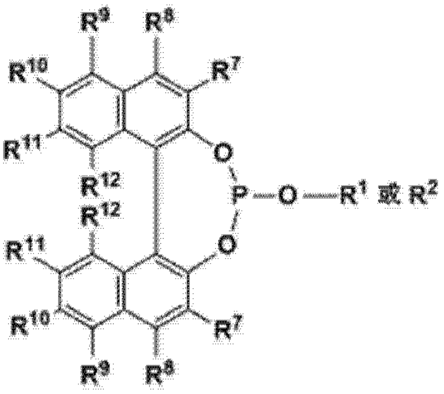
其中在结构 IX 中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；并且 $R^1$ 和 $R^2$ 彼此桥接或彼此不桥接；

其中为所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为 TLS 存在的磷的摩尔百分比规定预定极限值。

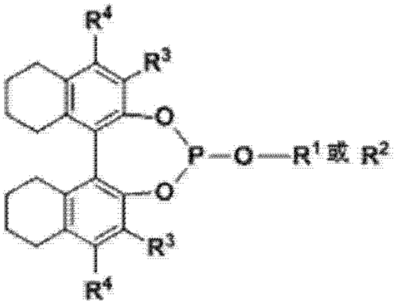
8. 根据权利要求 1 所述的方法，其中所述至少一种副产物包含 C-phite 配体结构（CLS），该 C-phite 配体结构具有如下显示为结构 VI、VII、或 VIII 的化学结构：



结构 VI

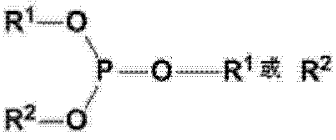


结构 VII



结构 VIII

其中所述至少一种副产物还包含 T-phite 配体结构（TLS），该 T-phite 配体结构具有如下显示为结构 IX 的化学结构：



结构 IX；

其中在结构 VI-VIII 和 IX 中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^1$ 和 $R^2$ 彼此桥接或彼此不桥接；并且 $R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和 $R^{12}$ 中的每一个独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团；

其中为所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比规定

预定极限值包括为所述最终反应混合物中作为TLS存在的磷的摩尔百分比规定预定极限值；

其中为所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为CLS存在的磷的摩尔百分比规定预定极限值。

9. 根据权利要求1所述的方法，其中所述至少一种副产物包含配体水解产物(LHP)，所述配体水解产物包含通过包括以下各项的过程得到的产物：

所述含磷配体或所述氯代亚磷酸酯的水解；

衍生自所述含磷配体或衍生自所述氯代亚磷酸酯的产物的水解；或

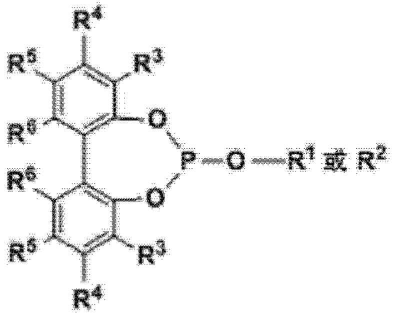
所述含磷配体的水解产物或所述氯代亚磷酸酯的水解产物的反应，或衍生自所述含磷配体或衍生自所述氯代亚磷酸酯的产物的水解产物的反应：

其中为所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为LHP存在的磷的摩尔百分比规定预定极限值。

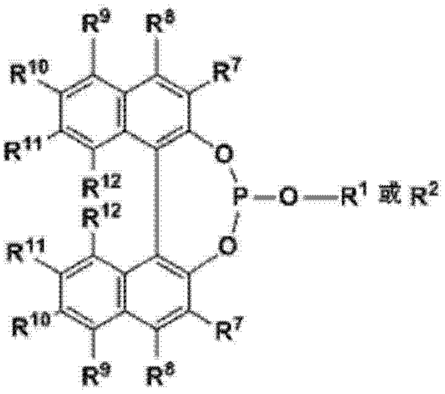
10. 根据权利要求9所述的方法，其中在所述最终反应混合物中，作为所述含磷配体结构存在的磷的百分比大于或等于约65％，并且作为所述LHP存在的磷的百分比小于不大于约5％。

11. 根据权利要求9所述的方法，其中在所述最终反应混合物中，作为所述含磷配体结构存在的磷的百分比大于或等于约70％，并且作为所述LHP存在的磷的百分比小于不大于约3.5％。

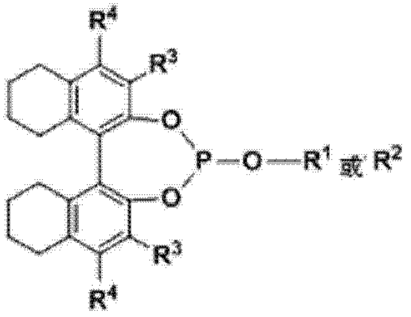
12. 根据权利要求1所述的方法，其中所述至少一种副产物包含C-phite配体结构(CLS)，该C-phite配体结构具有如下显示为结构VI、VII、或VIII的化学结构：



结构 VI

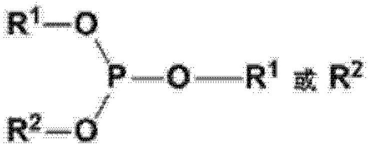


结构 VII



结构 VIII；

其中所述至少一种副产物还包含 T-phite 配体结构 (TLS)，该 T-phite 配体结构具有如下显示为结构 IX 的化学结构：



结构 IX；

其中在结构 VI-VIII 和 IX 中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^1$ 和 $R^2$ 彼此桥接或彼此不桥接；并且 $R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和 $R^{12}$ 中的每一个独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团；

其中为所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为 TLS 存在的磷的摩尔百分比规定预定极限值；

其中为所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为 CLS 存在的磷的摩尔百分比规定预定极限

值；

其中所述至少一种副产物还包含配体水解产物（LHP），所述配体水解产物包含通过包括以下各项的过程得到的产物：

所述含磷配体或所述氯代亚磷酸酯的水解；

衍生自所述含磷配体或衍生自所述氯代亚磷酸酯的产物的水解；或

所述含磷配体的水解产物或所述氯代亚磷酸酯的水解产物的反应，或衍生自所述含磷配体或衍生自所述氯代亚磷酸酯的产物的水解产物的反应；

其中为所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为LHP存在的磷的摩尔百分比规定预定极限值。

13. 根据权利要求1所述的方法，其中所述接触还包括利用所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值来确定要在所述第一或第二连续添加中添加的所述X-OH的量，以使作为所述至少一种副产物存在于所述第一或第二反应混合物中的磷的摩尔百分比小于所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值。

14. 根据权利要求2所述的方法，其中所述接触还包括利用所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值来确定要在所述第三连续添加中添加的所述X-OH的量，以使作为所述至少一种副产物存在于所述最终反应混合物中的磷的摩尔百分比小于所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值。

15. 根据权利要求1所述的方法，其中在所述第二连续添加中添加的所述X-OH的量小于在所述第一连续添加中添加的所述X-OH的量；并且其中在进行的情况下的所述第三连续添加中添加的所述X-OH的量等于或小于在所述第二连续添加中添加的所述X-OH的量。

16. 根据权利要求1所述的方法，其中在所述第二或第三连续添加中添加的所述X-OH的量为零。

17. 根据权利要求1所述的方法，其中如果在所述第二连续添加中添加的所述X-OH的量为零，则所述第二连续添加物包含水或所述具有化学结构$R^1$-OH或$R^2$-OH的醇中的至少一种；并且其中如果在所述第三连续添加中添加的所述X-OH的量为零，则在进行的情况下的所述第三连续添加物包含水或所述具有化学结构$R^1$-OH或$R^2$-OH的醇中的至少一种。

18. 根据权利要求4所述的方法，其中利用作为所述CLS存在于所述第一或第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值的比较以确定要在所述第二连续添加中或要在进行的情况下的所述第三连续添加中添加的化合物的量包括：在所述第二或第三添加中添加一定量的选自由所述X-OH、水、和所述具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，所述一定量足以使所述第二或最终反应混合物中作为所述CLS存在的磷的摩尔百分比等于或低于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值。

19. 根据权利要求18所述的方法，其中如果作为所述CLS存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含水或所述具有化学结构$R^1$-OH或$R^2$-OH的

醇；并且其中如果作为所述 CLS 存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三连续添加物包含水或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。

20. 根据权利要求 18 所述的方法，其中如果作为所述 CLS 存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含所述 X-OH；并且其中如果作为所述 CLS 存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三添加物不包含所述 X-OH。

21. 根据权利要求 7 所述的方法，其中利用作为所述 TLS 存在于所述第一或第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值的比较来确定要在所述第二或第三连续添加中添加的化合物的量包括：在所述第二或第三添加中添加一定量的选自由所述 X-OH、水、和所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，所述一定量足以使所述第二或最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比等于或低于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值。

22. 根据权利要求 21 所述的方法，其中如果作为所述 TLS 存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含水；并且其中如果作为所述 TLS 存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三连续添加物包含水。

23. 根据权利要求 21 所述的方法，其中如果作为 TLS 存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含所述 X-OH 或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇；并且其中如果作为 TLS 存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三连续添加物不包含所述 X-OH 或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。

24. 根据权利要求 9 所述的方法，其中利用作为所述 LHP 存在于所述第一或第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述 LHP 存在的磷的摩尔百分比的预定极限值的比较来确定要在所述第二或第三连续添加中添加的化合物的量包括：在所述第二或第三添加中添加一定量的选自由所述 X-OH、水、和所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，所述一定量足以使作为所述 LHP 存在于所述第二或最终反应混合物中的磷的摩尔百分比等于或低于所述最终反应混合物中作为所述 LHP 存在的磷的摩尔百分比的预定极限值。

25. 根据权利要求 24 所述的方法，其中如果作为 LHP 存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 LHP 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含所述 X-OH 或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇；并且其中如果作为 LHP 存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 LHP 存在的磷的摩尔百分比的预定极限值，则在进行的情

况下的所述第三连续添加物包含所述 X-OH 或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。

26. 根据权利要求 24 所述的方法，其中如果作为 LHP 存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 LHP 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含水；并且其中如果作为 LHP 存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 LHP 存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三连续添加物不包含水。

27. 根据权利要求 8 所述的方法，其中如果在所述第一反应混合物中作为所述 CLS 和所述 TLS 存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，则所述第二连续添加物包含水；并且其中如果在所述第二反应混合物中作为所述 CLS 和所述 TLS 存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，则在进行的情况下的所述第三连续添加物包含水。

28. 根据权利要求 8 所述的方法，其中如果在所述第一反应混合物中作为所述 CLS 和所述 TLS 存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，则所述第二连续添加物不包含所述 X-OH 或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇；并且其中如果在所述第二反应混合物中作为所述 CLS 和所述 TLS 存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，则在进行的情况下的所述第三连续添加物不包含所述 X-OH 或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。

29. 根据权利要求 1 所述的方法，其中所述接触还包括：

为所述第二反应混合物中氯代亚磷酸酯的转化率规定预定目标值；

在添加第一连续添加物之后，确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率；以及

在添加所述第二连续添加物之前，利用所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值的比较，以确定要在所述第二连续添加中添加的所述 X-OH 的量。

30. 根据权利要求 8 所述的方法，其中所述接触还包括：

为所述第二反应混合物中氯代亚磷酸酯的转化率规定预定目标值；

在添加第一连续添加物之后，确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率；以及

在添加所述第二连续添加物之前，利用所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值的比较，以确定要在所述第二连续添加中添加的所述 X-OH 的量。

31. 根据权利要求 30 所述的方法，其中如果在所述第一反应混合物中作为所述 CLS 或作为所述 TLS 存在的磷的摩尔百分比都不等于或不高于所述最终反应混合物中作为所述 CLS 或作为所述 TLS 存在的磷的摩尔百分比的相应预定极限值，并且所述第一反应混合物中氯代亚磷酸酯的转化率小于所述最终反应混合物中氯代亚磷酸酯的转化率的预定目标值，则要在所述第二连续添加中添加的所述 X-OH 的量足以使所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率等于或高于所述第二反应混合物中所述氯代亚磷酸酯的转

化率的预定目标值。

32. 根据权利要求 30 所述的方法，其中如果在所述第一反应混合物中作为所述 CLS 或作为所述 TLS 存在的磷的摩尔百分比都不等于或不高于所述最终反应混合物中作为所述 CLS 或作为所述 TLS 存在的磷的摩尔百分比的相应预定极限值，并且所述第一反应混合物中氯代亚磷酸酯的转化率小于所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值，则所述第二连续添加物不包含水或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。

33. 根据权利要求 1 或 29 所述的方法，其中如果所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率小于约 100％，则所述方法还包括将所述第三连续添加物添加至所述第二反应混合物，其中所述第三连续添加物包含足够量的水或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇，使得在第三连续添加之后，在所述最终反应混合物中的氯代亚磷酸酯转化率为约 100％。

34. 根据权利要求 7 所述的方法，所述方法还包括确定所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率，并且确定所述第二反应混合物中作为 TLS 存在的磷的摩尔百分比，其中如果所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率小于约 100％，并且如果在所述第二反应混合物中作为 TLS 存在的磷的摩尔百分比小于所述最终反应混合物中作为 TLS 存在的磷的摩尔百分比的预定极限值，则所述方法还包括将所述第三连续添加物添加至所述第二反应混合物，其中所述第三连续添加物包含足够量的所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇，使得在第三连续添加之后，在所述最终反应混合物中的所述氯代亚磷酸酯的转化率为约 100％。

35. 根据权利要求 9 所述的方法，其中如果所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率小于约 100％，并且如果在所述第二反应混合物中作为 LHP 存在的磷的摩尔百分比小于所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值，则所述方法还包括将第三连续添加物添加至所述第二反应混合物，其中所述第三连续添加物包含足够量的水，使得在第三连续添加之后，在所述最终反应混合物中的所述氯代亚磷酸酯的转化率为约 100％。

36. 根据权利要求 35 所述的方法，其中在所述第三连续添加之后，在所述最终反应混合物中作为所述含磷配体结构存在的磷的百分比大于或等于约 65％并且作为所述 LHP 存在的磷的百分比小于约 5％。

37. 根据权利要求 35 所述的方法，其中在所述第三连续添加之后，在所述最终反应混合物中作为所述含磷配体结构存在的磷的百分比大于或等于约 70％，并且作为所述 LHP 存在的磷的百分比小于约 3.5％。

38. 根据权利要求 1 所述的方法，其中所述接触还包括 ：

为所述第一反应混合物中氯代亚磷酸酯的转化率规定预定目标值 ；

在添加第一连续添加物之前，利用所述第一反应混合物中氯代亚磷酸酯的转化率的预定目标值，以确定要在所述第一连续添加中添加的所述 X-OH 的量，使得所述第一反应混合物中氯代亚磷酸酯的转化率等于或高于所述第一反应混合物中氯代亚磷酸酯的转化率的预定目标值。

39. 根据权利要求 9 所述的方法，其中所述接触还包括 ：

为所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比规定预定极限值 ；

在添加第一连续添加物之后，确定所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比；以及

在添加所述第二连续添加物之前，利用所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比与所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值的比较，以确定所述第二连续添加物的组成。

40. 根据权利要求 12 所述的方法，其中所述接触还包括：

为所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比规定预定极限值；

在添加第一连续添加物之后，确定所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比；以及

在添加所述第二连续添加物之前，利用所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比与所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值的比较，以确定所述第二连续添加物的组成。

41. 根据权利要求 40 所述的方法，其中如果在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比等于或大于所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。

42. 根据权利要求 40 所述的方法，其中如果在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比等于或大于所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含所述 X-OH 或水。

43. 根据权利要求 8 所述的方法，其中所述接触还包括：

为所述第二反应混合物中氯代亚磷酸酯的转化率规定预定目标值；以及

在添加第一连续添加物之后，

确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率；以及

其中如果在所述第一反应混合物中作为所述 CLS 和所述 TLS 存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，则所述第二连续添加物包含水；

其中如果在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含水或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇；并且

其中如果在所述第一反应混合物中作为所述 CLS 或作为所述 TLS 存在的磷的摩尔百分

比都不等于或不高于所述最终反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比的相应预定极限值，并且所述第一反应产物中氯代亚磷酸酯的转化率小于第二反应混合物中氯代亚磷酸酯的转化率的预定目标值，则所述第二连续包含足够量的所述X-OH，使得所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率等于或高于所述第二反应混合物中所述氯代亚磷酸酯的转化率的预定目标值。

44. 根据权利要求43所述的方法，其中如果在所述第一反应混合物中作为所述CLS存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含所述具有化学结构$R^1$-OH或$R^2$-OH的醇。

45. 根据权利要求12所述的方法，其中所述接触还包括：

为所述第二反应混合物中氯代亚磷酸酯的转化率规定预定目标值；以及

在添加第一连续添加物之后，

确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率；以及

确定所述第一反应混合物中作为LHP存在的磷的摩尔百分比；

其中如果在所述第一反应混合物中作为所述CLS和所述TLS存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比的相应预定极限值，则所述第二连续添加物包含水；

其中如果在所述第一反应混合物中作为所述CLS存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为LHP存在的磷的摩尔百分比等于或大于所述最终反应混合物中作为LHP存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含所述具有化学结构$R^1$-OH或$R^2$-OH的醇；并且

其中如果在所述第一反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比都不等于或不高于所述最终反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比的相应预定极限值，并且所述第一反应产物中氯代亚磷酸酯的转化率小于所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值，则第二连续添加物包含足够量的X-OH，使得所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率等于或高于所述第二反应混合物中所述氯代亚磷酸酯的转化率的预定目标值。

46. 根据权利要求45所述的方法，其中接触还包括：

其中如果在所述第一反应混合物中作为所述CLS存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为LHP存在的磷的摩尔百分比不等于或大于所述最终反应混合物中作为LHP存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含水或所述具有化学结构$R^1$-OH或$R^2$-OH的醇；并且

其中如果在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比不等于或大于所述最终反应混合物中 LHP 含量的预定极限值，则所述第二添加物包含水。

47. 根据权利要求 45 所述的方法，其中接触还包括：

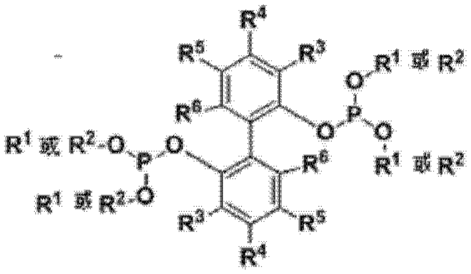
其中如果在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比不等于或大于所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含所述 X-OH；并且

其中如果在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比不等于或大于所述最终反应混合物中 LHP 含量的预定极限值，则所述第二添加物不包含水或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。

48. 根据权利要求 1 所述的方法，其中所述第一反应混合物具有化学计量过量的氯代亚磷酸酯。

49. 根据权利要求 1 所述的方法，其中所述接触在化学计量过量的有机叔胺的存在下进行。

50. 根据权利要求 1 所述的方法，其中所述含磷配体具有以下化学结构：

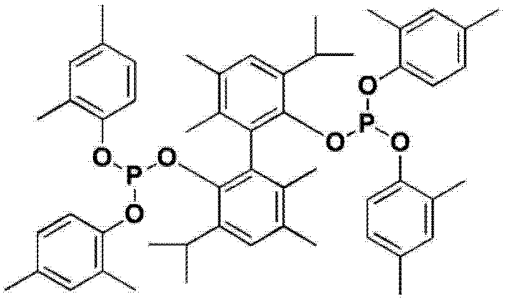


其中 $R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

51. 根据权利要求 1 所述的方法，其中 $R^2 = R^1$，其中 $R^1$ 是单价二甲苯基。

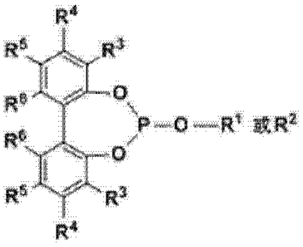
52. 根据权利要求 1 所述的方法，其中 $R^2 = R^1$，其中 $R^1$ 是单价 2,4- 二甲苯基。

53. 根据权利要求 1 所述的方法，其中所述含磷配体具有以下化学结构：



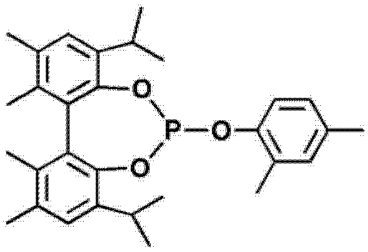
。

54. 根据权利要求 4 所述的方法，其中所述 CLS 具有以下化学结构：



其中 $R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

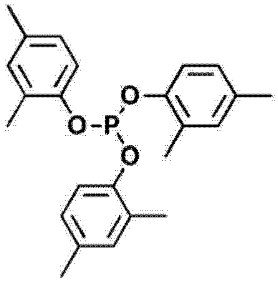
55. 根据权利要求 4 所述的方法，其中所述 CLS 具有以下化学结构：



。

56. 根据权利要求 7 所述的方法，其中所述 TLS 具有化学结构 $P(OR^1)_3$，其中 $R^1$ 是取代或未取代的芳基。

57. 根据权利要求 7 所述的方法，其中所述 TLS 具有以下化学结构：



。

58. 根据权利要求 1 的方法，其中所述有机叔胺包括三烷基胺。

59. 根据权利要求 1 的方法，其中所述有机叔胺包括三乙胺。

60. 根据权利要求 4 所述的方法，其中所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值小于或等于约 5%。

61. 根据权利要求 4 所述的方法，其中所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值小于或等于约 3%。

62. 根据权利要求 30、43、或 45 中任一项所述的方法，其中利用所述第一反应混合物中

所述氯代亚磷酸酯的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值的比较以确定要在所述第二连续添加中添加的所述 X-OH 的量包括：

利用在给定的转化率范围下的所述氯代亚磷酸酯至所述含磷配体和 CLS 的至少一个选择性比率来预测氯代亚磷酸酯的最大百分比转化率，使得在所述第二反应混合物中的所述预测的百分比转化率下，所述第二反应混合物中作为 CLS 存在的磷的百分比小于所述最终反应混合物中作为 CLS 存在的磷的百分比的预定极限值；

将所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值设定为所述氯代亚磷酸酯的所述预测的最大百分比转化率；以及

在所述第二连续添加中添加一定量的所述 X-OH，所述一定量足以使所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率约等于所述第二反应混合物中所述氯代亚磷酸酯的转化率的预定目标值。

63. 根据权利要求 62 所述的方法，其中在给定的转化率范围下的所述氯代亚磷酸酯至所述含磷配体和 CLS 的选择性比率包括对于至多约 98％的转化率而言约 1：6 的 CLS 与含磷配体的摩尔选择性比率。

64. 根据权利要求 62 所述的方法，其中在给定的转化率范围下的所述氯代亚磷酸酯至所述含磷配体和 CLS 的选择性比率包括对于约 98％至约 100％之间的转化率而言约 1：1 的 CLS 与含磷配体的摩尔选择性比率。

65. 根据权利要求 7 所述的方法，其中所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值小于或等于约 30％。

66. 根据权利要求 7 所述的方法，其中所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值小于或等于约 22％。

67. 根据权利要求 30、43、或 45 中任一项所述的方法，其中利用所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值的比较以确定要在所述第二连续添加中添加的所述 X-OH 的量包括：

利用在给定的转化率范围下的所述氯代亚磷酸酯至所述含磷配体和 TLS 的至少一个选择性比率来预测氯代亚磷酸酯的最大百分比转化率，使得在所述第二反应混合物中的所述预测的百分比转化率下，所述第二反应混合物中作为 TLS 存在的磷的百分比小于所述最终反应混合物中作为 TLS 存在的磷的百分比的预定极限值；

将所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值设定为所述氯代亚磷酸酯的所述预测的最大百分比转化率；以及

在所述第二连续添加中添加一定量的所述 X-OH，所述一定量足以使所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率约等于所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率的预定目标值。

68. 根据权利要求 67 所述的方法，其中在给定的转化率范围下的所述氯代亚磷酸酯至所述含磷配体和 CLS 的选择性比率包括对于至多约 98％的转化率而言约 1：6 的 CLS 与含磷配体的摩尔选择性比率。

69. 根据权利要求 67 所述的方法，其中在给定的转化率范围下的所述氯代亚磷酸酯至所述含磷配体和 CLS 的选择性比率包括对于约 98％至约 100％之间的转化率而言约 1：1 的 CLS 与含磷配体的摩尔选择性比率。

70. 根据权利要求29、30、43、或45中任一项所述的方法，其中所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值为约95％至约100％。

71. 根据权利要求29、30、43、或45中任一项所述的方法，其中所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值为约96％至约99％。

72. 根据权利要求38所述的方法，其中所述第一反应混合物中所述氯代亚磷酸酯的转化率的预定目标值为约85％至约95％。

73. 根据权利要求38所述的方法，其中所述第一反应混合物中所述氯代亚磷酸酯的转化率的预定目标值为约90％。

74. 根据权利要求39、40、或45中任一项所述的方法，其中所述最终反应混合物中作为LHP存在的磷的摩尔百分比的预定极限值为约5％。

75. 根据权利要求39、40、或45中任一项所述的方法，其中所述最终反应混合物中作为LHP存在的磷的摩尔百分比的预定极限值为约3％。

76. 根据权利要求1所述的方法，其中所述接触通过选自由以下步骤组成的组的至少一个步骤进行：

(i) 将所述X-OH进料至所述氯代亚磷酸酯和所述有机叔胺的混合物中；

(ii) 将所述X-OH和所述有机叔胺分别进料至所述氯代亚磷酸酯中；或

(iii) 将所述X-OH和所述有机叔胺以混合物形式进料至所述氯代亚磷酸酯中。

77. 根据权利要求1所述的方法，其中所述反应混合物还包含至少一种芳族烃溶剂。

78. 根据权利要求77所述的方法，其中所述芳族溶剂包括甲苯。

79. 根据权利要求77所述的方法，所述方法还包括将所述X-OH以包含所述X-OH和所述烃溶剂的溶液形式进料至所述氯代亚磷酸酯中。

80. 通过根据权利要求1所述的方法制备的结构I的含磷配体。

81. 根据权利要求1所述的方法，其中

第一连续添加物包含足够量的所述X-OH，使得所述第一反应混合物中所述氯代亚磷酸酯的转化率为约85％至约95％；并且

所述第二连续添加物包含比在所述第一连续添加中添加的所述X-OH的量更小的量的所述X-OH。

82. 根据权利要求1所述的方法，其中

第一连续添加物包含足够量的X-OH，使得所述第一反应混合物中所述氯代亚磷酸酯的转化率为约85％至约90％；并且

所述第二连续添加物包含足够量的所述具有化学结构$R^1$-OH或$R^2$-OH的醇，使得在所述第二反应混合物中的氯代亚磷酸酯转化率为约100％。

83. 根据权利要求1所述的方法，其中

第一连续添加物包含足够量的所述X-OH，使得所述第一反应混合物中所述氯代亚磷酸酯的转化率为约85％至约95％；并且

在所述第二连续添加之后，所述第二反应混合物中所述氯代亚磷酸酯的转化率为约95％至约99％；

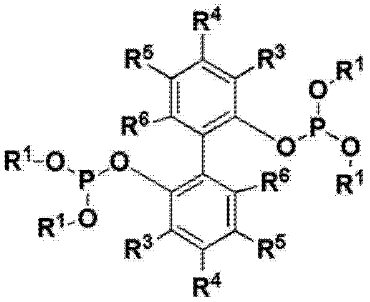
所述第三连续添加物包含足够量的水或所述具有化学结构$R^1$-OH或$R^2$-OH的醇，使得所述最终反应混合物中所述氯代亚磷酸酯的转化率为约100％。

84. 根据权利要求 1 所述的方法，其中所述方法提供作为第一最终反应混合物的最终反应混合物，其中重复所述方法以提供第二最终反应混合物，其中所述第一最终反应混合物中所述含磷配体的产率在所述第二最终反应混合物中所述含磷配体的产率的 5％之内。

85. 根据权利要求 4 所述的方法，其中所述方法提供作为第一最终反应混合物的最终反应混合物，其中重复所述方法以提供第二最终反应混合物，其中所述第一最终反应混合物中作为所述含磷配体、TLS、和 CLS 存在的磷的百分比各自分别在所述第二最终反应混合物中作为所述含磷配体、TLS、和 CLS 存在的磷的百分比的 5％之内。

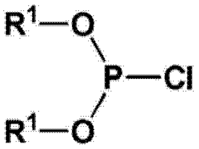
86. 根据权利要求 4 所述的方法，其中所述方法提供作为第一最终反应混合物的最终反应混合物，其中重复所述方法以提供第二最终反应混合物，其中所述第一最终反应混合物中作为 CLS 存在的磷的百分比在所述第二最终反应混合物中作为所述 CLS 存在的磷的百分比的 5％之内。

87. 一种用于制备具有以下结构的二亚磷酸酯配体结构 (DLS) 的方法，

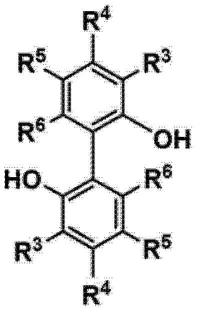


所述方法包括：

使具有以下结构的氯代亚磷酸酯，



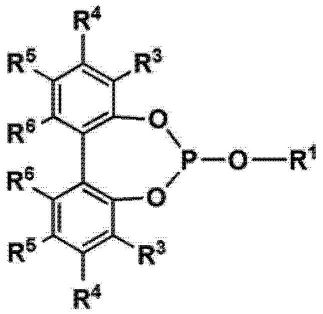
与具有以下结构的联芳化合物



和有机叔胺接触以提供包含所述二亚磷酸酯的最终反应混合物；

其中所述接触包括

为所述最终反应混合物中作为 C-phite 配体结构 (CLS) 存在的磷的摩尔百分比规定预定极限值，所述 C-phite 配体结构具有以下所示的化学结构：



在第一连续添加中将所述联芳化合物添加至所述氯代亚磷酸酯，使得在所述第一添加中添加的氯代亚磷酸酯的摩尔数大于在所述第一添加中添加的所述联芳化合物的摩尔数，以提供第一反应混合物；

确定作为CLS存在于所述第一反应混合物中的磷的摩尔百分比；

利用作为CLS存在于所述第一反应混合物中的磷的摩尔百分比与作为CLS存在的磷的摩尔百分比的预定极限值的比较，以确定要在第二连续添加中添加的选自由所述联芳化合物、水、和具有化学结构$R^1$-OH的醇中的至少一种组成的组的化合物的量，使得第二反应混合物中作为CLS存在的磷的摩尔百分比小于或等于所述最终反应混合物中作为CLS存在的磷的摩尔百分比的预定极限值；

向所述第一反应混合物添加第二连续添加物，包括选自由所述联芳化合物、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，以提供所述第二反应混合物；以及

或者

进行第三添加步骤，所述第三添加步骤包括

任选地确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比；

任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述X-OH、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物的量；以及

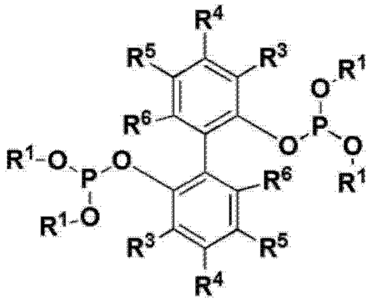
向所述第二反应混合物添加第三连续添加物，包括选自由所述X-OH、水、和所述具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，以提供最终反应混合物；

或者

所述最终反应混合物是所述第二反应混合物；

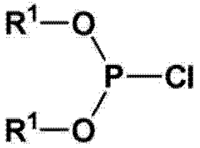
其中$R^1$和$R^2$是相同或不同的、取代或未取代的单价芳基；$R^3$、$R^4$、$R^5$、$R^6$中的每一个独立地选自由氢和$C_{1-10}$烷基组成的组。

88. 一种用于制备具有以下结构的二亚磷酸酯配体结构(DLS)的方法，

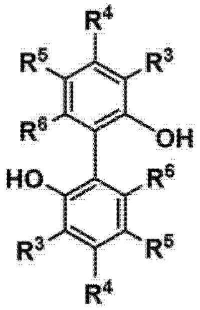


所述方法包括：

使具有以下结构的氯代亚磷酸酯，



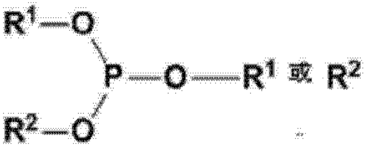
与具有以下结构的联芳化合物



和有机叔胺接触以提供包含所述二亚磷酸酯的最终反应混合物；

其中所述接触包括

为所述最终反应混合物中作为T-phite配体结构(TLS)存在的磷的摩尔百分比规定预定极限值，所述T-phite配体结构具有以下所示的化学结构



；

在第一连续添加中将所述联芳化合物添加至所述氯代亚磷酸酯，使得在所述第一添加中添加的氯代亚磷酸酯的摩尔数大于在所述第一添加中添加的联芳的摩尔数，以提供第一反应混合物；

确定作为TLS存在于所述第一反应混合物中的磷的摩尔百分比；

利用作为TLS存在于所述第一反应混合物中的磷的摩尔百分比与作为TLS存在的磷的摩尔百分比的预定极限值的比较，以确定要在第二连续添加中添加的选自由所述联芳化合物、水、和具有化学结构$R^1$-OH的醇组成的组的化合物的量，使得第二反应混合物中作为TLS存在的磷的摩尔百分比小于或等于所述最终反应混合物中作为TLS存在的磷的摩尔百分比的预定极限值；

向所述第一反应混合物添加第二连续添加物，包括选自由所述联芳化合物、水、和具有

化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供所述第二反应混合物；以及

或者

进行第三添加步骤，所述第三添加步骤包括

任选地确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比；

任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述 X-OH、水、和所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量；以及

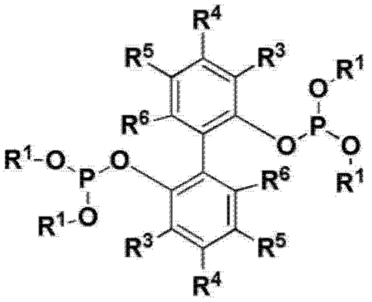
向所述第二反应混合物添加第三连续添加物，包括选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供最终反应混合物；

或者

所述最终反应混合物是所述第二反应混合物；

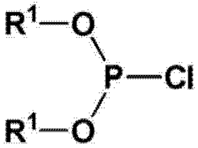
其中 $R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；并且 $R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

89. 一种用于制备具有以下结构的二亚磷酸酯配体结构 (DLS) 的方法，

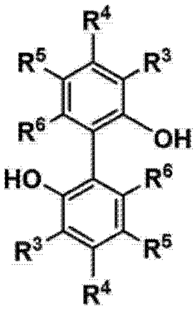


所述方法包括：

使具有以下结构的氯代亚磷酸酯，



与具有以下结构的联芳化合物



和有机叔胺接触以提供包含所述二亚磷酸酯的最终反应混合物；

其中所述接触包括

为所述最终反应混合物中作为配体水解产物 (LHP) 存在的磷的摩尔百分比规定预定

极限值，所述配体水解产物包含通过包括以下各项的过程得到的产物：

所述 DLS 或所述氯代亚磷酸酯的水解；

衍生自所述 DLS 或衍生自所述氯代亚磷酸酯的产物的水解；或

所述 DLS 的水解产物或所述氯代亚磷酸酯的水解产物的反应，或衍生自所述 DLS 或衍生自所述氯代亚磷酸酯的产物的水解产物的反应；

在第一连续添加中将所述联芳化合物添加至所述氯代亚磷酸酯，使得在所述第一添加中添加的氯代亚磷酸酯的摩尔数大于在所述第一添加中添加的联芳的摩尔数，以提供第一反应混合物；

确定作为 LHP 存在于所述第一反应混合物中的磷的摩尔百分比；

利用作为 LHP 存在于所述第一反应混合物中的磷的摩尔百分比与作为 LHP 存在的磷的摩尔百分比的预定极限值的比较，以确定要在第二连续添加中添加的选自由所述联芳化合物、水、和具有化学结构 $R^1$-OH 的醇组成的组的化合物的量，使得第二反应混合物中作为 LHP 存在的磷的摩尔百分比小于或等于所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值；

向所述第一反应混合物添加第二连续添加物，包括选自由所述联芳化合物、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供所述第二反应混合物；以及

或者

进行第三添加步骤，所述第三添加步骤包括

任选地确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比；

任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量；以及

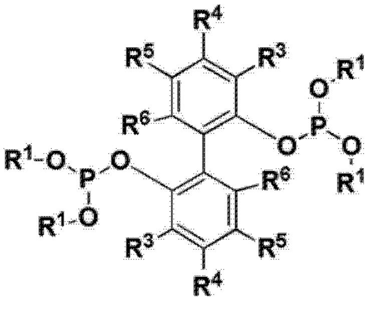
向所述第二反应混合物添加第三连续添加物，包括选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供最终反应混合物；

或者

所述最终反应混合物是所述第二反应混合物；

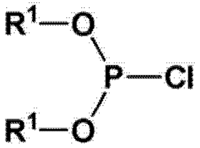
其中 $R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；并且 $R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

90. 一种用于制备具有以下结构的二亚磷酸酯配体结构 (DLS) 的方法，

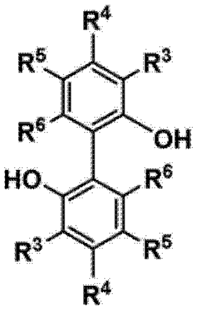


所述方法包括：

使具有以下结构的氯代亚磷酸酯，



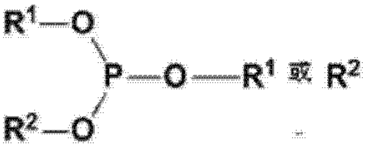
与具有以下结构的联芳化合物



和有机叔胺接触以提供包含所述二亚磷酸酯的最终反应混合物；

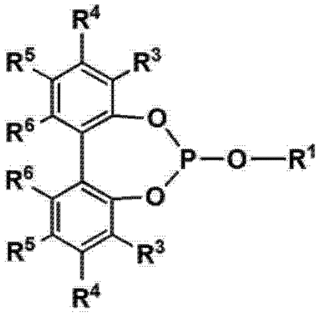
其中所述接触包括

为所述最终反应混合物中作为T-phite配体结构（TLS）存在的磷的摩尔百分比规定预定极限值，所述T-phite配体结构具有以下所示的化学结构



；

为所述最终反应混合物中作为C-phite配体结构（CLS）存在的磷的摩尔百分比规定预定极限值，所述C-phite配体结构具有以下所示的化学结构：



为所述最终反应混合物中作为配体水解产物（LHP）存在的磷的摩尔百分比规定预定极限值，所述配体水解产物包含通过包括以下各项的过程得到的产物：

所述DLS或所述氯代亚磷酸酯的水解；

衍生自所述DLS或衍生自所述氯代亚磷酸酯的产物的水解；或

所述DLS的水解产物或所述氯代亚磷酸酯的水解产物的反应，或衍生自所述DLS或衍生自所述氯代亚磷酸酯的产物的水解产物的反应；

为所述第一反应混合物中氯代亚磷酸酯的转化率规定预定目标值；

在第一连续添加中将所述联芳化合物添加至所述氯代亚磷酸酯，以提供第一反应混合物，其中添加的联芳化合物的量足以使所述第一反应混合物中所述氯代亚磷酸酯的百分比

转化率等于或大于所述第一反应混合物中所述氯代亚磷酸酯的转化率的预定目标值；

确定作为 TLS 存在于所述第一反应混合物中的磷的摩尔百分比；

确定作为 CLS 存在于所述第一反应混合物中的磷的摩尔百分比；

确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率；

其中如果在所述第一反应混合物中作为所述 CLS 和所述 TLS 存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，则所述第二连续添加物包含水；

其中如果在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比等于或大于所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇；

其中如果在所述第一反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比都不等于或不高于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，并且第一反应产物中氯代亚磷酸酯的转化率小于第二反应混合物中氯代亚磷酸酯的转化率的预定目标值，则第二连续添加物包含所述联芳化合物，其中要在所述第二连续添加中添加的所述联芳化合物的量通过以下方式确定：利用所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值的比较，以确定要在所述第二连续添加中添加的所述联芳化合物的量，包括：

将在给定的转化率范围下的所述氯代亚磷酸酯至所述含磷配体和 CLS 的至少一个选择性比率与所述第一反应混合物中 TLS 和 CLS 的确定的摩尔百分比组合利用，以预测氯代亚磷酸酯的最大百分比转化率，使得在所述第二反应混合物中的所述预测的百分比转化率下，所述第二反应混合物中作为 CLS 存在的磷的百分比小于所述最终反应混合物中作为 CLS 存在的磷的百分比的预定极限值；以及

将所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值设定为所述氯代亚磷酸酯的所述预测的最大百分比转化率；

向所述第一反应混合物添加所述第二连续添加物，包括选自由所述联芳化合物、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供所述第二反应混合物，其中如果在所述第二连续添加中添加联芳化合物，则所述第二连续添加中所述联芳化合物的量足以使所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率约等于所述第二反应混合物中所述氯代亚磷酸酯的转化率的预定目标值；以及

或者

进行第三添加步骤，所述第三添加步骤包括

任选地确定作为至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比；

任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由水和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量；以及

将第三连续添加物添加至所述第二反应混合物以提供所述最终反应混合物，其中在所述第三添加中添加的一种或多种化合物的量使得所述最终反应混合物中所述氯代亚磷酸酯的转化率为约 100％；

或者

所述最终反应混合物是所述第二反应混合物，其中在所述第二添加中添加的一种或多种化合物的量使得所述最终反应混合物中所述氯代亚磷酸酯的转化率为约 100％；

其中 $R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；并且 $R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

# 特征在于测量副产物水平以确定进一步添加的由氯代亚磷酸酯制备有机二亚磷酸酯的方法

## 发明领域

[0001] 本发明涉及用于含磷配体结构的合成的方法。

[0002] 发明背景

[0003] 在尼龙的生产中的关键中间体是己二腈(ADN)。ADN商业上通过1,3-丁二烯和3-戊烯腈(3PN)在包含镍(0)和亚磷酸酯配体的催化剂的存在下的氢氰化而制备。商业上使用的亚磷酸酯配体是单齿亚磷酸酯如亚磷酸三芳基酯,其形成充当用于反应的催化剂前体的镍-配体配合物。尽管有用,但是单齿亚磷酸酯可能导致较低催化剂活性和较高的镍消耗。

[0004] 近来,镍催化剂活性以及3PN和ADN的收率的显著提升已经通过使用包含镍(0)和作为配体的双齿亚磷酸酯的催化剂而实现。双齿亚磷酸酯配体通常含有2个磷给体原子,其可以与单个过渡金属形成环状螯合物结构。

[0005] 结构通式为$(RO)_2P(OZO)P(OR)_2$的双齿亚磷酸酯,在本文中也称为二亚磷酸酯,是特别令人感兴趣的。传统上,这样的二亚磷酸酯可以通过以下方法合成:由$PCl_3$与ROH在有机叔胺的存在下的反应制备氯代亚磷酸酯$(RO)_2PCl$。然后,在后续反应中,双官能醇,如HO-Z-OH,可以与氯代亚磷酸酯在另外的有机叔胺的存在下反应,提供$(RO)_2P(OZO)P(OR)_2$。有机叔胺能够通过形成有机叔胺盐酸盐来中和在两个反应步骤中的HCl副产物。ROH和HO-Z-OH的性质以及每一个反应步骤所选择的条件可以影响所需产物的选择性。

[0006] 例如,美国专利5,235,113和WO96/22968公开了二亚磷酸酯的合成。美国专利5,235,113公开了用于制备结构$(RO)_2P(OAO)P(OR)_2$的二亚磷酸酯的方法,其中A为联苯基并且R为3,6-二-叔丁基-2-萘基。WO96/22968公开了$(ArO)_2P(OZO)P(OAr)_2$类型的多齿亚磷酸酯化合物的合成,其中Ar和Z是取代或未取代的芳基。

[0007] 美国专利6,069,267提供了通式$(R^1O)_2P(OZO)P(OR^1)_2$的有机二亚磷酸酯的制备方法,其中$R^1$和Z是不同的取代或未取代的芳基。

[0008] WO2004/050588公开了低于0℃,例如介于0℃至-20℃之间的产物混合物的低温和粘度显著增加操作成本和工艺复杂性。

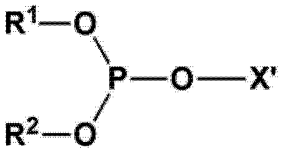
[0009] WO2004/091780还描述了通过以下方式制备包含结构式$(R^1O)_2P(OZO)P(OR^1)_2$的双齿亚磷酸酯配体的粗制配体混合物的方法:在有机碱的存在下,使温度在约-25℃至约+35℃之间的包含$(R^1O)_2PCl$的第一反应产物与约一半摩尔当量的HO-Z-OH接触。

[0010] WO2010/123743和WO2010/123747描述了用于制备有机二亚磷酸酯的方法的实例。

[0011] 发明概述

[0012] 本发明的多个实施方案提供用于制备具有以下化学结构的含磷配体结构的方法

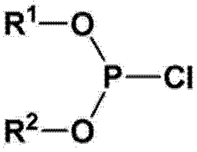
[0013]



结构 I'

[0014] 所述方法包括，使以下结构的氯代亚磷酸酯，

[0015]

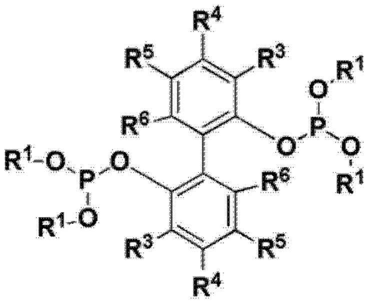


结构 II

[0016] 与具有化学结构 X-OH 的化合物和有机叔胺接触以提供包含所述含磷配体结构的最终反应混合物。所述接触包括，为所述最终反应混合物中作为至少一种副产物存在的磷的摩尔百分比规定预定极限值。所述接触还包括，在第一连续添加中将所述 X-OH 添加至所述氯代亚磷酸酯中，以提供第一反应混合物。所述接触还包括，确定作为所述至少一种副产物存在于所述第一反应混合物中的磷的摩尔百分比。所述接触还包括，利用作为所述至少一种副产物存在于所述第一反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第二连续添加中添加的选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量。所述接触还包括，向所述第一反应混合物添加第二连续添加物，包括选自由所述 X-OH、水、或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供第二反应混合物。所述接触还包括进行第三添加步骤，或者所述最终反应混合物是所述第二反应混合物。在进行的情况下的所述第三添加步骤包括，任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量。在进行的情况下的所述第三添加步骤包括，任选地确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比。在进行的情况下的所述第三添加步骤还包括，向所述第二反应混合物添加第三连续添加物，包括选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供最终反应混合物。在本段中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^1$ 和 $R^2$ 彼此桥接或彼此不桥接；并且 X 和 X' 中的每一个独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、亚磷酸酯基（phosphityl）联芳基、亚磷酸酯基联杂芳基、羟基联芳基、羟基联杂芳基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团。

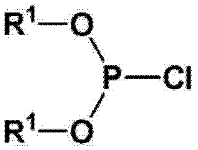
[0017] 本发明的多个实施方案提供用于制备具有以下结构的二亚磷酸酯配体结构（DLS）的方法，

[0018]



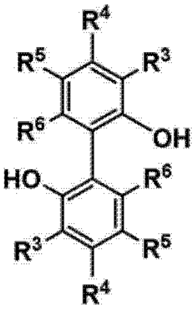
[0019] 所述方法包括，使具有以下结构的氯代亚磷酸酯，

[0020]



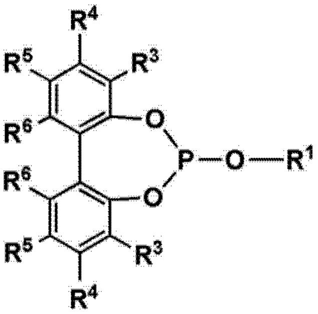
[0021] 与具有以下结构的联芳化合物、

[0022]



[0023] 和有机叔胺接触以提供包含所述二亚磷酸酯的最终反应混合物。所述接触包括，为所述最终反应混合物中作为 C-phite 配体结构 (CLS) 存在的磷的摩尔百分比规定预定极限值，所述 C-phite 配体结构具有以下所示的化学结构 ：

[0024]



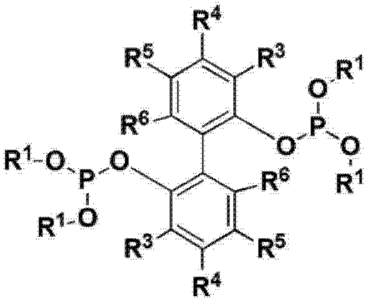
。

[0025] 所述接触还包括，在第一连续添加中将所述联芳化合物添加至所述氯代亚磷酸酯，使得在所述第一添加中添加的氯代亚磷酸酯的摩尔数大于在所述第一添加中添加的所述联芳化合物的摩尔数，以提供第一反应混合物。所述接触还包括，确定作为 CLS 存在于所述第一反应混合物中的磷的摩尔百分比。所述接触还包括，利用作为 CLS 存在于所述第一反应混合物中的磷的摩尔百分比与作为 CLS 存在的磷的摩尔百分比的预定极限值的比较，来确定要在第二连续添加中添加的选自由所述联芳化合物、水、和具有化学结构 $R^1$-OH 的醇中的至少一种组成的组的化合物的量，使得第二反应混合物中作为 CLS 存在的磷的摩尔百

分比小于或等于所述最终反应混合物中作为 CLS 存在的磷的摩尔百分比的预定极限值。所述接触还包括，向所述第一反应混合物添加第二连续添加物，包括选自由所述联芳化合物、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供所述第二反应混合物。所述接触还包括进行第三添加步骤，或者所述最终反应混合物是所述第二反应混合物。在进行的情况下的所述第三添加步骤包括，任选地确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比。在进行的情况下的所述第三添加步骤包括，任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量。在进行的情况下的所述第三添加步骤包括，向所述第二反应混合物添加第三连续添加物，包括选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供最终反应混合物。在本段中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

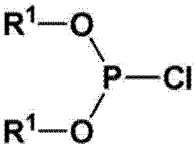
[0026] 本发明的多个实施方案提供用于制备具有以下结构的二亚磷酸酯配体结构 (DLS) 的方法，

[0027]



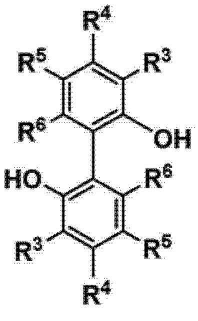
[0028] 所述方法包括，使具有以下结构的氯代亚磷酸酯，

[0029]



[0030] 与具有以下结构的联芳化合物、

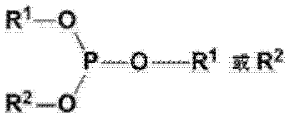
[0031]



[0032] 和有机叔胺接触以提供包含所述二亚磷酸酯的最终反应混合物。所述接触包括，为所述最终反应混合物中作为 T-phite 配体结构 (TLS) 存在的磷的摩尔百分比规定预定极

限值，所述 T-phite 配体结构具有以下所示的化学结构

[0033]



。

[0034] 所述接触还包括，在第一连续添加中将所述联芳化合物添加至所述氯代亚磷酸酯，使得在所述第一添加中添加的氯代亚磷酸酯的摩尔数大于在所述第一添加中添加的联芳的摩尔数，以提供第一反应混合物。所述接触还包括，确定作为 TLS 存在于所述第一反应混合物中的磷的摩尔百分比。所述接触还包括，利用作为 TLS 存在于所述第一反应混合物中的磷的摩尔百分比与作为 TLS 存在的磷的摩尔百分比的预定极限值的比较，来确定要在第二连续添加中添加的选自由所述联芳化合物、水、和具有化学结构 $R^1$-OH 的醇组成的组的化合物的量，使得第二反应混合物中作为 TLS 存在的磷的摩尔百分比小于或等于所述最终反应混合物中作为 TLS 存在的磷的摩尔百分比的预定极限值。所述接触还包括，向所述第一反应混合物添加第二连续添加物，包括选自由所述联芳化合物、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供所述第二反应混合物。所述接触还包括进行第三添加步骤，或者所述最终反应混合物是所述第二反应混合物。在进行的情况下的所述第三添加步骤包括，任选地确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比。在进行的情况下的所述第三添加步骤还包括，任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量。在进行的情况下的所述第三添加步骤还包括，向所述第二反应混合物添加第三连续添加物，包括选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供最终反应混合物。在本段中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；并且 $R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

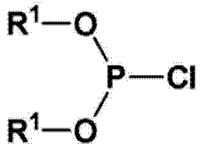
[0035] 本发明的多个实施方案提供用于制备具有以下结构的二亚磷酸酯配体结构 (DLS) 的方法，

[0036]

。

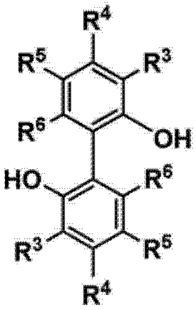
[0037] 所述方法包括，使具有以下结构的氯代亚磷酸酯，

[0038]



[0039]　与具有以下结构的联芳化合物、

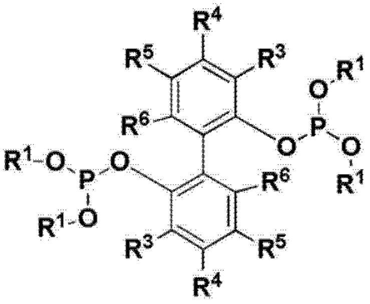
[0040]



[0041]　和有机叔胺接触以提供包含所述二亚磷酸酯的最终反应混合物。所述接触包括，为所述最终反应混合物中作为配体水解产物(LHP)存在的磷的摩尔百分比规定预定极限值。所述 LHP 包含至少一种通过包括以下各项的过程得到的产物：所述 DLS 或所述氯代亚磷酸酯的水解；衍生自所述 DLS 或所述氯代亚磷酸酯的产物的水解；或所述 DLS 的或所述氯代亚磷酸酯的水解产物的反应，或衍生自所述 DLS 或所述氯代亚磷酸酯的产物的水解产物的反应。所述接触包括，在第一连续添加中将所述联芳化合物添加至所述氯代亚磷酸酯，使得在所述第一添加中添加的氯代亚磷酸酯的摩尔数大于在所述第一添加中添加的联芳的摩尔数，以提供第一反应混合物。所述接触包括，确定作为 LHP 存在于所述第一反应混合物中的磷的摩尔百分比。所述接触包括，利用作为 LHP 存在于所述第一反应混合物中的磷的摩尔百分比与作为 LHP 存在的磷的摩尔百分比的预定极限值的比较，来确定要在第二连续添加中添加的选自由所述联芳化合物、水、和具有化学结构 $R^1$-OH 的醇组成的组的化合物的量，使得第二反应混合物中作为 LHP 存在的磷的摩尔百分比小于或等于所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值。所述接触包括，向所述第一反应混合物添加第二连续添加物，包括选自由所述联芳化合物、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供所述第二反应混合物。所述接触还包括进行第三添加步骤，或者所述最终反应混合物是所述第二反应混合物。在进行的情况下的所述第三添加步骤包括，任选地确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比。在进行的情况下的所述第三添加步骤包括，任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量。在进行的情况下的所述第三添加步骤还包括，向所述第二反应混合物添加第三连续添加物，包括选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供最终反应混合物。在本段中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；并且 $R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

[0042]　本发明的多个实施方案提供用于制备具有以下结构的二亚磷酸酯配体结构(DLS)的方法，

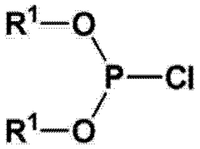
[0043]



。

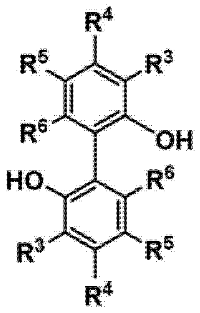
[0044] 所述方法包括，使具有以下结构的氯代亚磷酸酯，

[0045]



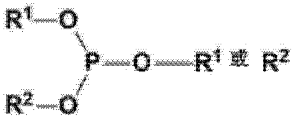
[0046] 与具有以下结构的联芳化合物、

[0047]



[0048] 和有机叔胺接触以提供包含所述二亚磷酸酯的最终反应混合物。所述接触包括，为所述最终反应混合物中作为 T-phite 配体结构 (TLS) 存在的磷的摩尔百分比规定预定极限值，所述 T-phite 配体结构具有以下所示的化学结构

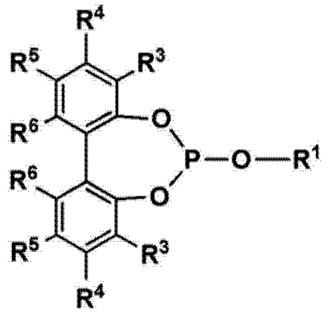
[0049]



。

[0050] 所述接触还包括，为所述最终反应混合物中作为 C-phite 配体结构 (CLS) 存在的磷的摩尔百分比规定预定极限值，所述 C-phite 配体结构具有以下所示的化学结构

[0051]



。

[0052] 所述接触还包括，为所述最终反应混合物中作为配体水解产物(LHP)存在的磷的摩尔百分比规定预定极限值。LHP包含至少一种通过包括以下各项的过程得到的产物：所述DLS或所述氯代亚磷酸酯的水解；衍生自所述DLS或所述氯代亚磷酸酯的产物的水解；或所述DLS的或所述氯代亚磷酸酯的水解产物的反应，或衍生自所述DLS或所述氯代亚磷酸酯的产物的水解产物的反应。所述接触还包括，为所述第一反应混合物中氯代亚磷酸酯的转化率规定预定目标值。所述接触还包括，在第一连续添加中将所述联芳化合物添加至所述氯代亚磷酸酯，以提供第一反应混合物，其中添加的联芳化合物的量足以使所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率等于或大于所述第一反应混合物中所述氯代亚磷酸酯的转化的所述预定目标值。所述接触还包括，确定作为TLS存在于所述第一反应混合物中的磷的摩尔百分比。所述接触还包括，确定作为CLS存在于所述第一反应混合物中的磷的摩尔百分比。所述接触还包括，确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率。如果在所述第一反应混合物中作为所述CLS和所述TLS存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比的相应预定极限值，则所述第二连续添加物包含水。如果在所述第一反应混合物中作为所述CLS存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为LHP存在的磷的摩尔百分比等于或大于所述最终反应混合物中作为LHP存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含具有化学结构$R^1$-OH或$R^2$-OH的醇。如果在所述第一反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比都不等于或不高于所述最终反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比的相应预定极限值，并且所述第一反应产物中氯代亚磷酸酯的所述转化率小于第二反应混合物中氯代亚磷酸酯的所述转化率的所述预定目标值，则第二连续添加物包含所述联芳化合物，其中在所述第二连续添加中添加的所述联芳化合物的量通过以下方法确定：利用所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的所述转化率的所述预定目标值的比较，来确定要在所述第二连续添加中添加的所述联芳化合物的量。利用比较来确定要在所述第二连续添加中添加的联芳化合物的量包括，利用在给定的转化率范围的所述氯代亚磷酸酯至所述含磷配体和CLS的至少一个选择性比率与所述第一反应混合物中TLS和CLS的确定的摩尔百分比结合来预测氯代亚磷酸酯的最大百分比转化率，使得在所述第二反应混合物中所述预测的转化率下，所述第二反应混合物中作为CLS存在的磷的百分比小于所述最终反应混合物中作为CLS存在的磷的百分比的预定极限值。利用比较来确定要在所述第二连续添加中添加

的联芳化合物的量还包括，将第二反应混合物中氯代亚磷酸酯的所述转化率的预定目标值设定为所述氯代亚磷酸酯的所述预测的最大百分比转化率。所述接触还包括，向所述第一反应混合物添加第二连续添加物，包括选自由所述联芳化合物、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供所述第二反应混合物，其中如果在所述第二连续添加中添加联芳化合物，则所述第二连续添加中所述联芳化合物的量足以使所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率约等于所述第二反应混合物中所述氯代亚磷酸酯的所述转化率的预定目标值。所述接触还包括进行第三添加步骤，或者所述最终反应混合物是所述第二反应混合物。如果所述最终反应混合物是所述第二反应混合物，在所述第二添加中添加的所述一种或多种化合物的量使得所述最终反应混合物中所述氯代亚磷酸酯的转化率为约 100％。如果进行，第三添加步骤包括，任选地确定作为至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比。如果进行，第三添加步骤包括，任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由水和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量。如果进行，第三添加步骤还包括，将所述第三连续添加物添加至所述第二反应混合物以提供所述最终反应混合物，其中在所述第三添加中添加的所述一种或多种化合物的量使得所述最终反应混合物中所述氯代亚磷酸酯的所述转化率为约 100％。在本段中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；并且 $R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

[0053] 本发明提供优于其他制备含磷配体的方法的某些优点，所述含磷配体包括含二亚磷酸酯配体结构 (DLS)。在一些实施方案中，以比其他方法更高的产率生成含磷配体或 DLS。在多个实施方案中，生成具有比其他方法更小量的杂质的含磷配体，例如可以生成具有比其他方法更小量的 TLS 或 CLS 的 DLS。在一些实施方案中，在最终产物混合物中，可以生成具有比其他方法更小量的水解产物的含磷配体。例如，在最终产物混合物中，可以生成具有比其他方法更小量的配体水解产物 (LHP) 的 DLS。在一些实施方案中，可以生成具有比其他方法更高度受控的量的杂质和水解产物的含磷配体。例如，可以生成具有比其他方法更高度受控的量的 TLS、CLS、或 LHP 的 DLS。在一些实施方案中，在最终产物混合物中，杂质或水解产物以在最大浓度的指定的极限值内存在，同时含磷配体的产率高于其他可以将杂质或水解产物保持在相似的极限值内的方法的产率。例如，在最终产物混合物中，TLS、CLS、和 LHP 可以以在最大浓度的指定的极限值内存在，同时 DLS 的产率可以高于其他可以将 TLS、CLS、和 LHP 保持在相似的极限值内的方法的产率。在一些实施方案中，含有含磷配体的最终产物混合物具有足够低浓度的杂质或水解产物，使得可以使用最终产物混合物生成配合物，所述配合物可以比通过其他含磷配体合成方法的最终产物混合物形成的催化剂更有效地发挥作为催化剂的功能。例如，含有 DLS 的最终产物混合物可以具有足够低浓度的 TLS、CLS、或 LHP，使得可以使用最终产物混合物生成镍 (0)-DLS 配合物，所述镍 (0)-DLS 配合物可以比通过其他 DLS 合成方法的最终产物混合物形成的镍 (0)-DLS 配合物更有效地发挥作为氢氰化催化剂的功能。在一些实施方案中，最终产物混合物可以具有足够低浓度的杂质或水解产物，使得可以使用其生成可以有效地催化特定反应的催化剂，同时含磷配体的总产率可以高于用于制备包含含磷配体并且可以生成有效用于催化特定反应的催

化剂的最终反应混合物的其他方法的总产率。例如，最终产物混合物可以具有足够低浓度的 TLS、CLS、或 LHP，使得可以使用其生成可以有效地发挥作为氢氰化催化剂的功能的镍(0)-DLS 配合物，同时 DLS 的总产率可以高于用于制备可以形成有效用于催化氢氰化反应的镍 (0)-DLS 配合物的含 DLS 最终产物混合物的其他方法的总产率。在多个实施方案中，可以始终重复所述方法以产生具有在规格极限值(specification limit)内的杂质水平的最终反应混合物。在一些实例中，可以始终重复所述方法以产生具有高度一致的杂质水平和含磷配体产率的最终反应混合物。在一些实例中，可以始终重复所述方法以产生具有在规格极限值内、高度一致的 CLS 副产物水平的最终反应混合物。在一些实施方案中，在氢氰化反应中使用后可以有效地回收含磷配体或由配体制备的催化剂配合物，同时维持比通过其他方法制备的含磷配体或由其制备的配合物更高的催化效率。本发明的多个实施方案满足对用于制备包括 DLS 在内的含磷配体的简易和选择性的方法的需要，所述含磷配体满足预定的纯度规格，包括用于作为氢氰化催化剂的组分的用途。在获得对含磷配体如 DLS 的形成的高选择性的同时，本发明的一些实施方案提供用于克服其他方法如在美国专利号 6,069,267 和 WO2004/050588 中确定的那些方法的温度限制的方法。

[0054] 发明详述

[0055] 现在将详细参考所公开的主题的某些权利要求。尽管将与列举的权利要求一起描述所公开的主题，应理解的是它们并非意在将所公开的主题限制为那些权利要求。相反，所公开的主题意在涵盖全部替代物、修改、和等价物，它们可以包括在由权利要求所定义的本公开主题的范围内。

[0056] 在说明书中提及“一个实施方案”、“实施方案”、“实例实施方案”等，表示所描述的实施方案可以包括特定的特征、结构、或特性，但是每个实施方案可以并非必须包括特定的特征、结构、或特性。此外，此类短语并非必须指代相同的实施方案。此外，当与实施方案一起描述特定的特征、结构、或特性时，应该认为无论是否明确地描述，与其他实施方案一起实施这种特征、结构、或特性都是在本领域技术人员的知识范围之内的。

[0057] 在本文献中，除非另外指出，术语“一个”或“一种”用于包括一种或多于一种，并且术语“或”用于指代非排他性的“或”。此外，应该理解的是，在本文中采用的、并且没有另外定义的语法或术语仅用于描述目的而不是限制的目的。任何的章节标题的使用都是意在辅助文献的阅读而不应被解释为限制；与章节标题有关的信息可以发生在特定的章节之内或之外。此外，在本文献中提及的全部出版物、专利、和专利文献通过引用将其全部内容结合在本文中，如同通过引用单独结合一样。在本文献与通过引用这样结合的那些文献之间用法不一致的情况下，在所结合的参考文献中的用法应该被认为是本文献的用法的补充；对于不可调和的矛盾，以本文献中的用法为准。

[0058] 在本文中所描述的制备方法中，除了在明确地叙述时间或操作顺序时之外，步骤可以按任何顺序进行而不背离本发明的原理。在权利要求中叙述以便首先进行一个步骤、然后接着进行多个其他步骤，应当用来意指第一步在其他步骤中的任何一个之前进行，但是其他步骤可以按任何适合的顺序进行，除非在其他步骤内也叙述了顺序。例如，叙述“步骤 A、步骤 B、步骤 C、步骤 D、和步骤 E”的权利要求要素应被解释为意指首先进行步骤 A，最后进行步骤 E，并且步骤 B、C、和 D 可以在步骤 A 和 E 之间按任何顺序进行，并且顺序仍然落在要求保护的方法的字面范围内。还可以重复、或与其他步骤同时进行给定的步骤或步骤

的子组。在另一个实例中，叙述“步骤A、步骤B、步骤C、步骤D、和步骤E”的权利要求要素可以被解释为意指首先进行步骤A，接着进行步骤B，接着进行步骤C，接着进行步骤D，并且最后进行步骤E。

[0059] 此外，可以同时进行指定的步骤，除非明确的权利要求语言叙述它们是单独进行的。例如，完成X的要求保护的步骤和完成Y的要求保护的步骤可以在单一操作内同时进行，并且得到的方法将会落在要求保护的工艺的字面范围内。

[0060] 定义

[0061] 单数形式“一个”、“一种”、和“所述”可以包括复数的所指对象，除非上下文明确地另外指出。

[0062] 术语“约”可以允许数值或范围的一定程度的变化，例如，在所述的数值的或范围的所述的界限的10％内、5％内、或1％内。当给定一定范围的或一列的连续数值时，除非另外指定，在所述范围内的任何数值或在给定的连续数值之间的任何数值也是公开的。

[0063] 如在本文中所使用的术语“有机基团”是指，但不限于，任何含碳官能团。例如，含氧基团如烷氧基、芳氧基、芳烷氧基、氧代基（羰基）、羧基（包括羧酸、羧酸盐、和羧酸酯）；含硫基团如烷基硫醚基和芳基硫醚基；以及其他含有杂原子的基团。有机基团的非限制性实例包括OR′、OC(O)N(R′)$_2$、CN、CF$_3$、OCF$_3$、R′、C(O)、亚甲二氧基、亚乙二氧基、N(R′)$_2$、SR′、SOR′、SO$_2$R′、SO$_2$N(R′)$_2$、SO$_3$R′、C(O)R′、C(O)C(O)R′、C(O)CH$_2$C(O)R′、C(S)R′、C(O)OR′、OC(O)R′、C(O)N(R′)$_2$、OC(O)N(R′)$_2$、C(S)N(R′)$_2$、(CH$_2$)$_{0-2}$N(R′)C(O)R′、(CH$_2$)$_{0-2}$N(R′)N(R′)$_2$、N(R′)N(R′)C(O)R′、N(R′)N(R′)C(O)OR′、N(R′)N(R′)CON(R′)$_2$、N(R′)SO$_2$R′、N(R′)SO$_2$N(R′)$_2$、N(R′)C(O)OR′、N(R′)C(O)R′、N(R′)C(S)R′、N(R′)C(O)N(R′)$_2$、N(R′)C(S)N(R′)$_2$、N(COR′)COR′、N(OR′)R′、C(＝NH)N(R′)$_2$、C(O)N(OR′)R′、或C(＝NOR′)R′其中R’可以是氢（在包含其他碳原子的实例中）或基于碳的部分，并且其中基于碳的部分本身可以是被进一步取代的；例如，其中R’可以是氢（在包含其他碳原子的实例中）、烷基、酰基、环烷基、芳基、芳烷基、杂环基、杂芳基、或杂芳烷基，其中任何烷基、酰基、环烷基、芳基、芳烷基、杂环基、杂芳基、或杂芳烷基、或R’可以独立地被J单取代或多取代；或者其中结合至一个氮原子或多个相邻的氮原子的两个R’基团可以与所述一个或多个氮原子一起形成杂环基，其可以被J单取代或独立地多取代。有机基团的实例包括直链和／或支链基团如烷基、完全或部分卤素取代的卤代烷基、烯基、炔基、芳基、丙烯酸酯官能团、和甲基丙烯酸酯官能团；以及其他有机官能团如醚基、氰酸酯基、酯基、羧酸盐基团、和被掩蔽的异氰基。有机基团的实例包括，但不限于，烷基如甲基、乙基、丙基、异丙基、正丁基、仲丁基、和叔丁基，丙烯酸酯官能团如丙烯酰氧基丙基和甲基丙烯酰氧基丙基；烯基如乙烯基、烯丙基、和丁烯基；炔基如乙炔基和丙炔基；芳基如苯基、甲苯基、和二甲苯基；氰基烷基如氰基乙基和氰基丙基；卤代烃基如3,3,3-三氟丙基、3-氯丙基、二氯苯基、和6,6,6,5,5,4,4,3,3-九氟己基；烯氧基聚（氧化烯）基如烯丙基氧基（聚氧乙烯）基、烯丙基氧基聚（氧丙烯）基、和烯丙基氧基-聚（氧丙烯）-共-聚（氧乙烯）基；烷氧基聚（氧化烯）基如丙氧基（聚氧乙烯）基、丙氧基聚（氧丙烯）基、和丙氧基-聚（氧丙烯）-共-聚（氧乙烯）基；卤素取代的烷氧基聚（氧化烯）基如全氟丙氧基（聚氧乙烯）基、全氟丙氧基聚（氧丙烯）基、和全氟丙氧基-聚（氧丙烯）-共-聚（氧乙烯）基；烷氧基如甲氧基、乙氧基、正丙氧基、异丙氧基、正丁氧基、和乙基己氧基；氨

基烷基如 3- 氨基丙基、6- 氨基己基、11- 氨基十一烷基、3-(N- 烯丙基氨基 ) 丙基、N-(2- 氨基乙基 )-3- 氨基丙基、N-(2- 氨基乙基 )-3- 氨基异丁基、对氨基苯基、2- 乙基吡啶基、和 3- 丙基吡咯基 ;环氧烷基如 3- 缩水甘油氧基丙基、2-(3,4,- 环氧环己基 ) 乙基、和 5,6- 环氧己基 ;酯官能团如乙酰氧乙基和苯甲酰氧丙基 ;羟基官能团如 2- 羟乙基 ;被掩蔽的异氰酸酯官能团如丙基 - 叔丁基氨基甲酸酯基、和丙基乙基氨基甲酸酯基 ;醛官能团如十一醛基和丁醛基 ;酸酐官能团如 3- 丙基琥珀酸酐基和 3- 丙基马来酸酐基 ;以及羧酸的金属盐如 3- 羧基丙基和 2- 羧基乙基的锌盐、钠盐、或钾盐。

[0064]　如在本文中所使用的术语“取代的”是指如在本文中定义的有机基团或在其中一个或多个连接包含在其中的氢原子的键被一个或多个连接非氢原子的键代替的分子。如在本文中所使用的术语“官能团”或“取代基”是指在分子上、或在有机基团上可以取代的或取代的基团。取代基或官能团的实例包括，但不限于，卤素 ( 例如，F、Cl、Br、和 I) ;基团如羟基、烷氧基、芳氧基、芳烷氧基、氧代基 ( 羰基 )、羧基 ( 包括羧酸、羧酸盐、和羧酸酯 ) 中的氧原子 ;基团如硫醇基、烷基硫醚基和芳基硫醚基、亚砜基、砜基、磺酰基、和磺酰胺基中的硫原子 ;基团如胺基、羟胺基、腈基、硝基、N- 氧化物、酰肼、叠氮化物、和烯胺中的氮原子 ;以及多种其他基团中的其他杂原子。可以结合至取代的碳 ( 或其他 ) 原子的取代基 J 的非限制性实例包括 F、Cl、Br、I、OR′ 、$OC(O)N(R')_2$、CN、NO、$NO_2$、$ONO_2$、叠氮基、$CF_3$、$OCF_3$、R′ 、O( 氧代基 )、S( 硫羰基 )、C(O)、S(O)、亚甲二氧基、亚乙二氧基、$N(R')_2$、SR′ 、SOR′ 、$SO_2R'$ 、$SO_2N(R')_2$、$SO_3R'$ 、C(O)R′ 、C(O)C(O)R′ 、$C(O)CH_2C(O)R'$ 、C(S)R′ 、C(O)OR′ 、OC(O)R′ 、$C(O)N(R')_2$、$OC(O)N(R')_2$、$C(S)N(R')_2$、$(CH_2)_{0-2}N(R')C(O)R'$ 、$(CH_2)_{0-2}N(R')N(R')_2$、N(R′ )N(R′ )C(O)R′ 、N(R′ )N(R′ )C(O)OR′ 、$N(R')N(R')CON(R')_2$、$N(R')SO_2R'$ 、$N(R')SO_2N(R')_2$、N(R′ )C(O)OR′ 、N(R′ )C(O)R′ 、N(R′ )C(S)R′ 、$N(R')C(O)N(R')_2$、$N(R')C(S)N(R')_2$、N(COR′ )COR′ 、N(OR′ )R′ 、$C(=NH)N(R')_2$、C(O)N(OR′ )R′ 、或 C( ＝ NOR′ )R′ ，其中 R’可以是氢或基于碳的部分，并且其中基于碳的部分本身可以是被进一步取代的 ;例如，其中 R’ 可以是氢、烷基、酰基、环烷基、芳基、芳烷基、杂环基、杂芳基、或杂芳烷基，其中任何烷基、酰基、环烷基、芳基、芳烷基、杂环基、杂芳基、或杂芳烷基、或 R’ 可以独立地被 J 单取代或多取代 ;或者其中结合至一个氮原子或多个相邻的氮原子的两个 R’基团可以与所述一个或多个氮原子一起形成杂环基，其可以被 J 单取代或独立地多取代。

[0065]　如在本文中所使用的术语“烷基”是指具有 1 至约 20 个碳原子的直链和支链烷基和环烷基，并且通常为 1 至 12 个碳或者，在一些实施方案中，为 1 至 8 个碳原子。直链烷基的实例包括具有 1 至 8 个碳原子的那些直链烷基如甲基、乙基、正丙基、正丁基、正戊基、正己基、正庚基、和正辛基。支链烷基的实例包括，但不限于，异丙基、异丁基、仲丁基、叔丁基、新戊基、异戊基、和 2,2- 二甲基丙基。如在本文中所使用的，术语“烷基”包括正烷基、异烷基、和反异烷基 (anteisoalkyl) 基团以及其他支链形式的烷基。代表性的取代的烷基可以被在本文中列出的任何基团取代一次或多次，例如，氨基、羟基、氰基、羧基、硝基、硫基、烷氧基、和卤素基团。

[0066]　如在本文中所使用的术语“烯基”是指如在本文中定义的直链和支链以及环状烷基，不同之处在于至少一个双键存在于两个碳原子之间。因此，烯基具有 2 至约 20 个碳原子，并且通常为 2 至 12 个碳或者，在一些实施方案中，为 2 至 8 个碳原子。实例包括，但不

限于乙烯基、$-CH=CH(CH_3)$、$-CH=C(CH_3)_2$、$-C(CH_3)=CH_2$、$-C(CH_3)=CH(CH_3)$、$-C(CH_2CH_3)=CH_2$、环己烯基、环戊烯基、环己二烯基、丁二烯基、戊二烯基、和己二烯基等。

[0067] 如在本文中所使用的术语“炔基”是指直链和支链烷基，不同之处在于至少一个三键存在于两个碳原子之间。因此，炔基具有2至约20个碳原子，并且通常为2至12个碳或者，在一些实施方案中，为2至8个碳原子。实例包括，但不限于$-C\equiv CH$、$-C\equiv C(CH_3)$、$-C\equiv C(CH_2CH_3)$、$-CH_2C\equiv CH$、$-CH_2C\equiv C(CH_3)$、和$-CH_2C\equiv C(CH_2CH_3)$等。

[0068] 如在本文中所使用的术语“酰基”是指含有羰基部分的基团，其中所述基团经由羰基碳原子结合。羰基碳原子还结合至另一个碳原子，其可以是烷基、芳基、芳烷基、环烷基、环烷基烷基、杂环基、杂环烷基、杂芳基、杂芳烷基等的一部分。在其中羰基碳原子结合至氢的特殊情况下，所述基团是“甲酰基”基团，作为该术语的酰基在本文中定义。酰基可以包含0至约12-20个额外的结合至羰基的碳原子。酰基可以包含在本文的含义内的双键或三键。丙烯酰基是酰基的实例。酰基还可以包含本文的含义内的杂原子。烟酰基（吡啶基-3-羰基）是在本文的含义内的酰基的实例。其他实例包括乙酰基、苯甲酰基、苯乙酰基、吡啶乙酰基(pyridylacetyl)、肉桂酰基、和丙烯酰基等。当含有结合至羰基碳原子的碳原子的基团含有卤素时，所述基团被称为“卤酰基”基团。实例是三氟乙酰基。

[0069] 如在本文中所使用的术语“环烷基”是指环状烷基如，但不限于，环丙基、环丁基、环戊基、环己基、环庚基、和环辛基。在一些实施方案中，环烷基可以具有3至约8-12个环成员，然而在其他实施方案中，环碳原子的数量范围为3至4、5、6、或7。环烷基还包括多环环烷基如，但不限于，降冰片基、金刚烷基、冰片基、莰烯基、异莰烯基、和蒈烯基，以及稠合环如，但不限于，十氢化萘基等。环烷基还包括被如在本文中定义的直链或支链烷基取代的环。代表性的取代的环烷基可以是单取代的或多次取代的，如，但不限于，2,2-，2,3-，2,4-2,5-或2,6-二取代的环己基或单取代的、二取代的或三取代的降冰片基或环庚基，它们可以被例如氨基、羟基、氰基、羧基、硝基、硫基、烷氧基、和卤素基团取代。术语“环烯基”单独或组合表示环状烯基。

[0070] 如在本文中所使用的术语“芳基”是指在环中不含杂原子的环状芳族烃。因此芳基包括，但不限于，苯基、甘菊环基、庚搭烯基、联苯基、茚基(indacenyl)、芴基、菲基、苯并菲基、芘基、并四苯基、䓛基、联苯撑基、蒽基、和萘基。在一些实施方案中，芳基在基团的环部分含有约6至约14个碳。如在本文中定义的，芳基可以是未取代的或取代的。代表性的取代的芳基可以是单取代的或多次取代的，如，但不限于，2-、3-、4-、5-、或6-取代的苯基或2-8取代的萘基，它们可以被碳或非碳基团（如在本文中列出的那些）取代。

[0071] 如在本文中所使用的术语“杂芳基”是指含有5个以上环成员的芳环化合物，其中，一个或多个是杂原子如，但不限于，N、O、和S；例如，杂芳基环可以具有5至约8-12个环成员。杂芳基是一种杂环基，其具有芳族电子结构。被指定为$C_2$-杂芳基的杂芳基可以是具有两个碳原子和三个杂原子的5元环、具有两个碳原子和四个杂原子的6元环等。同样地，$C_4$-杂芳基可以是具有一个杂原子的5元环、具有两个杂原子的6元环等。碳原子的数量加上杂原子的数量总和等于环原子的总数量。杂芳基包括，但不限于，以下基团如吡咯基、吡唑基、三唑基、四唑基、噁唑基、异噁唑基、噻唑基、吡啶基、噻吩基、苯并噻吩基、苯并呋喃基、吲哚基、氮杂吲哚基、吲唑基、苯并咪唑基、氮杂苯并咪唑基、苯并噁唑基、苯并噻唑基、

苯并噻二唑基、咪唑并吡啶基、异噁唑并吡啶基、硫杂萘基 (thianaphthalenyl)、嘌呤基、黄嘌呤基、腺嘌呤基、鸟嘌呤基、喹啉基、异喹啉基、四氢喹啉基、喹喔啉基、和喹唑啉基。杂芳基可以是未取代的，或者可以是被如在本文中讨论的基团取代的。代表性的取代的杂芳基可以被如在本文中列出的那些基团取代一次或多次。

[0072] 如在本文中所使用的术语“烷氧基”是指氧原子连接至烷基，包括在本文中定义的环烷基。直链烷氧基的实例包括但不限于甲氧基、乙氧基、丙氧基、丁氧基、戊氧基、己氧基等。支链烷氧基的实例包括但不限于异丙氧基、仲丁氧基、叔丁氧基、异戊氧基、异己氧基等。环状烷氧基的实例包括但不限于环丙氧基、环丁氧基、环戊氧基、环己氧基等。烷氧基可以包含一个至约 12-20 个结合至氧原子的碳原子，并且还可以包含双键或三键，并且还可以包含杂原子。例如，烯丙基氧基是在本文的含义内的烷氧基。甲氧基乙氧基也是在本文的含义内的烷氧基，如在上下文中的亚甲二氧基，其中结构的两个相邻原子被其取代。

[0073] 如在本文中所使用的术语“胺”是指伯胺、仲胺、和具有例如式 N(基团)$_3$ 的叔胺，其中每个基团可以独立地为 H 或非 H，如烷基、芳基等。胺包括但不限于 R-NH$_2$，例如，烷基胺、芳基胺、烷基芳基胺 ；R$_2$=H，其中每个 R 独立地选择，如二烷基胺、二芳基胺、芳基烷基胺、杂环基胺等 ；以及 R$_3$N，其中每个 R 独立地选择，如三烷基胺、二烷基芳基胺、烷基二芳基胺、三芳基胺等。术语“胺”还包括如在本文中所使用的铵离子。

[0074] 如在本文中所使用的术语“氨基”是指 -NH$_2$、-NHR、-NR$_2$、-NR$_3^+$ 形式的取代基，其中每个 R 独立地选择，以及除不能质子化的 -NR$_3^+$ 外的各自的质子化形式。因此，任何被氨基取代的化合物都可以被认为是胺。在本文的含义内的“氨基”可以是伯氨基、仲氨基、叔氨基或季氨基。“烷基氨基”包括单烷基氨基、二烷基氨基、和三烷基氨基。

[0075] 如在本文中所使用的术语“卤代”或“卤素”或“卤化物”，除非另外说明，其本身或作为另一种取代基的一部分意指氟原子、氯原子、溴原子、或碘原子，优选氟、氯、或溴。

[0076] 如在本文中所使用的术语“卤代烷基”基团包括单卤代烷基、其中所有卤代原子可以相同或不同的多卤代烷基，以及其中所有氢原子被卤素原子如氟取代的全卤代烷基。卤代烷基的实例包括三氟甲基、1，1- 二氯乙基、1，2- 二氯乙基、1，3- 二溴 -3，3- 二氟丙基、全氟丁基等。

[0077] 如在本文中所使用的术语“单价”是指经由单键连接至被取代的分子的取代基。当取代基是单价，如，例如，F 或 Cl 时，其结合至通过单键被其取代的原子。

[0078] 如在本文中所使用的术语“烃”是指包含碳和氢原子的官能团或分子。所述术语还可以指正常情况下包含碳和氢原子二者但是其中所有氢原子被其他官能团取代的官能团或分子。

[0079] 如在本文中所使用的术语“溶剂”是指可以溶解固体、液体、或气体的液体。溶剂的非限制性实例是有机化合物、水、醇、离子液体、和超临界流体。

[0080] 如在本文中所使用的术语“独立地选自”是指所指代的基团是相同的、不同的、或它们的混合物，除非上下文明确地另外指出。因此，在此定义下，短语“X$^1$、X$^2$、和 X$^3$ 独立地选自稀有气体”将会包括以下情况 ：例如，其中 X$^1$、X$^2$、和 X$^3$ 全部相同的情况，其中 X$^1$、X$^2$、和 X$^3$ 全部不同的情况，其中 X$^1$ 和 X$^2$ 是相同的但是 X$^3$ 是不同的情况，以及其他相似的变换的情况。

[0081] 如在本文中所使用的术语“配体”是指可以结合至中心金属原子 ( 例如 Ni(0)) 以

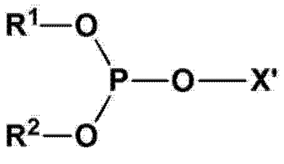
形成配位配合物（例如Ni(0)与DLS之间的配合物）的离子或分子。

[0082] 用于本方法的化学反应的短语“所述接触的阶段”通常的含义是：其中所述接触的初始阶段是所有三种反应物，即氯代亚磷酸酯，联芳化合物和有机叔胺首先接触的时候，并且最终阶段是反应终止的时候，例如，将水加入至反应混合物中以将有机叔胺盐酸盐与二亚磷酸酯分离的时候。

[0083] 概括

[0084] 本发明的多个方法提供用于制备具有以下化学结构的含磷配体结构的方法

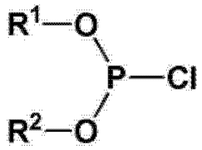
[0085]



结构 I'

[0086] 所述方法可以包括，使以下结构的氯代亚磷酸酯，

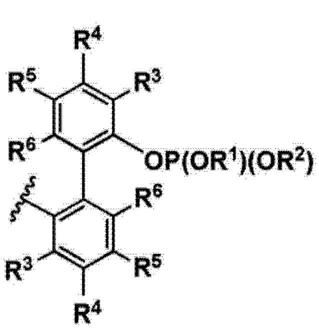
[0087]

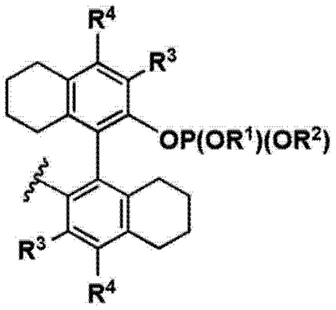


结构 II

[0088] 与具有化学结构X-OH的化合物和有机叔胺接触以提供包含所述配体结构的最终反应混合物。所述接触包括，为所述最终反应混合物中作为至少一种副产物存在的磷的摩尔百分比规定预定极限值。所述接触可以包括，在第一连续添加中将所述X-OH添加至所述氯代亚磷酸酯中，以提供第一反应混合物。所述接触可以包括，向所述第一反应混合物添加第二连续添加物，包括选自由所述X-OH、水、或所述具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，以提供第二反应混合物。所述接触还可以包括添加第三添加物，或者所述第二反应混合物是最终反应混合物。在进行的情况下的所述第三添加可以包括，添加选自由所述X-OH、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，以提供最终反应混合物。在最终反应混合物中，作为至少一种副产物存在的磷的百分比可以等于或低于最终反应混合物中作为至少一种副产物存在的磷的摩尔百分比的预定极限值。在本段中，$R^1$和$R^2$是相同或不同的、取代或未取代的单价芳基；$R^1$和$R^2$彼此桥接或彼此不桥接；并且X、X'、$R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和$R^{12}$中的每一个独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、亚磷酸酯基联芳基、亚磷酸酯基联杂芳基、羟基联芳基、羟基联杂芳基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团。在其中X＝亚磷酸酯基联芳基的多个实施方案中，在一些实例中，X可以具有选自以下结构中的一个的化学结构：

[0089]



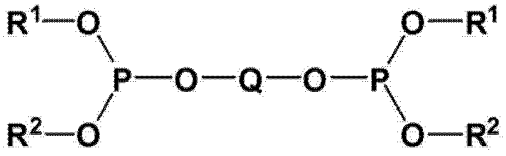


,

[0090] 其中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^1$ 和 $R^2$ 彼此桥接或彼此不桥接；并且 $R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和 $R^{12}$ 中的每一个独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团。

[0091] 在多个实施方案中，本发明提供制备含磷配体的方法，其中结构 I’ 的所述配体结构可以是具有结构 I 的化学结构的二亚磷酸酯配体结构（DLS），

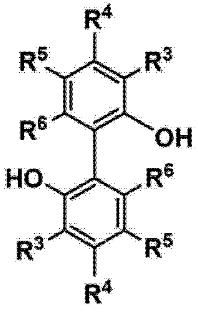
[0092]



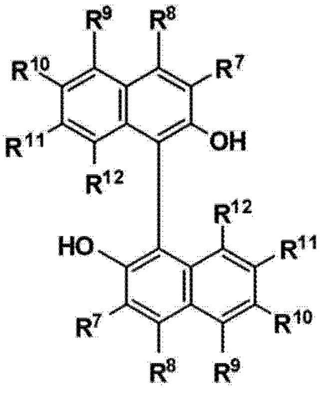
结构 I

[0093] 其中所述 X-OH 可以是选自由结构 III、结构 IV 和结构 V 组成的组的联芳化合物，

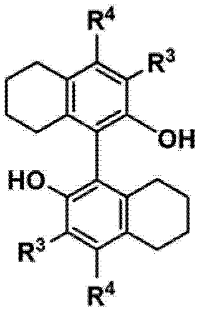
[0094]



结构 III



结构 IV



结构 V。

[0095] 在本段中给出的结构中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和 $R^{12}$ 中的每一个独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团；并且 O-Q-O 是联芳化合物的二价物种。

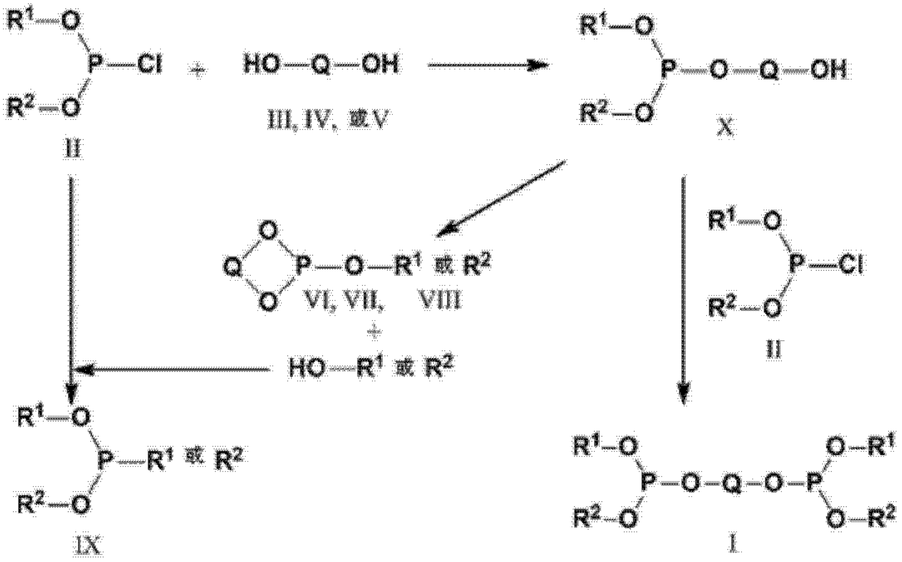
[0096] 在本文给出的结构中，除非另外指定，X 和 $R^1$-$R^{12}$ 独立地选自任何适合的官能团。在本文中提供了多个实例，包括在其中制备 DLS 的本发明的具体实施方案。然而，应该理解的是，用于 DLS 制备的方法是本发明的方法的具体实施方案，并且并非将其限制于此；相反，本发明一般提供制备含磷配体的方法。

[0097] 在本文中提供了所述方法的许多具体实例，包括其中 DLS 是含磷配体的实例。这些实例并非意在以任何方式限制本发明；本发明包括如在本文中所描述的用于任何适合的含磷配体的制备的方法。

[0098] 一般反应、C-phite配体结构(CLS)、T-Phite配体结构(TLS)、配体水解产物(LHP)

[0099] 方案 I 说明了所述方法的具体实施方案的总体反应方案，其中生成的含磷配体是 DLS。本领域技术人员将会容易地理解方案 I 中所示的具体实施方案采用具有 X-OH 结构(其中 X = -Q-OH) 的化合物，并且将能够容易地由所示的具体反应方案推断出使用 X-OH 代替 HO-Q-OH 的一般反应方案。方案 I 示出了，结构 X 的单亚磷酸酯中间体，和分别具有结构 VI、VII、和 VIII 的 C-phite 配体结构 (CLS) 的、以及具有结构 IX 的 T-phite 配体结构 (TLS) 的环状和非环状的单齿亚磷酸三有机酯副产物。$R^1$ 和 $R^2$ 可以是相同或不同的、取代或未取代的单价芳基。例如，$R^1$ 和 $R^2$ 可以是取代的或未取代的苯基、萘基、蒽基、和菲基。

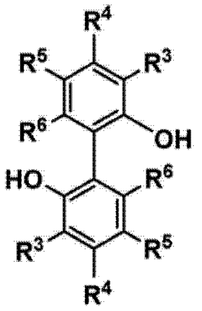
[0100]

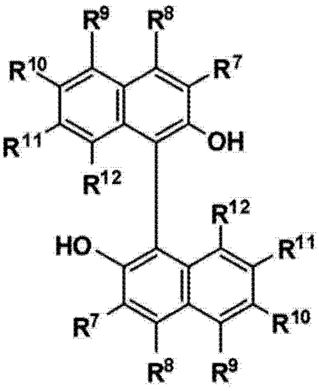


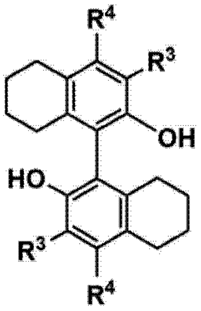
方案 I

[0101] 联芳化合物 HO-Q-OH 可以具有下列结构，

[0102]


结构 III


结构 IV


结构 V

[0103]　其中 $R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和 $R^{12}$ 中的每一个可以是任何适合的官能团。在一个实例中，$R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和 $R^{12}$ 独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团；并且 O-Q-O 是联芳化合物的二价物种。在一个实例中，$R^3$ 至 $R^{12}$ 可以是直链、支链、和环状 $C_1$ 至 $C_{18}$ 烷基；取代的或未取代的 $C_6$ 至 $C_{18}$ 芳基；取代的或未取代的 $C_6$ 至 $C_{18}$ 芳氧基；直链、支链、和环状 $C_1$ 至 $C_{18}$ 烷氧基；直链和支链 $C_2$ 至 $C_{18}$ 烷氧基烷基；取代的或未取代的 $C_3$ 至 $C_{18}$ 环状缩醛；取代的或未取代的 $C_7$ 至 $C_{18}$ 芳氧羰基；直链、支链、和环状 $C_2$ 至 $C_{18}$ 烷氧羰基；取代的或未取代的 $C_7$ 至 $C_{18}$ 芳基羰基；和取代的或未取代的 $C_2$ 至 $C_{18}$ 烷基羰基。

[0104]　在方案 I 中所示的总体反应方案的第一步骤中，氯代亚磷酸酯（结构 II）与联芳化合物 HO-Q-OH（具有结构 III，IV 或 V）反应，以得到单亚磷酸酯中间体（结构 X）。可以存在适合的包含碱性氮原子或多个氮原子的有机叔胺，如三有机胺或芳族叔胺，以中和由氯代亚磷酸酯与联芳化合物的反应形成的酸（HCl）。单亚磷酸酯中间体（结构 X）然后可以与氯代亚磷酸酯发生分子间反应，以得到所需的 DLS（结构 I），或它可以发生分子内反应以制备结构 VI、VII、和 VIII 的环状亚磷酸三有机酯副产物，其在本文中被称为 C-phite 配体结构、或 CLS。

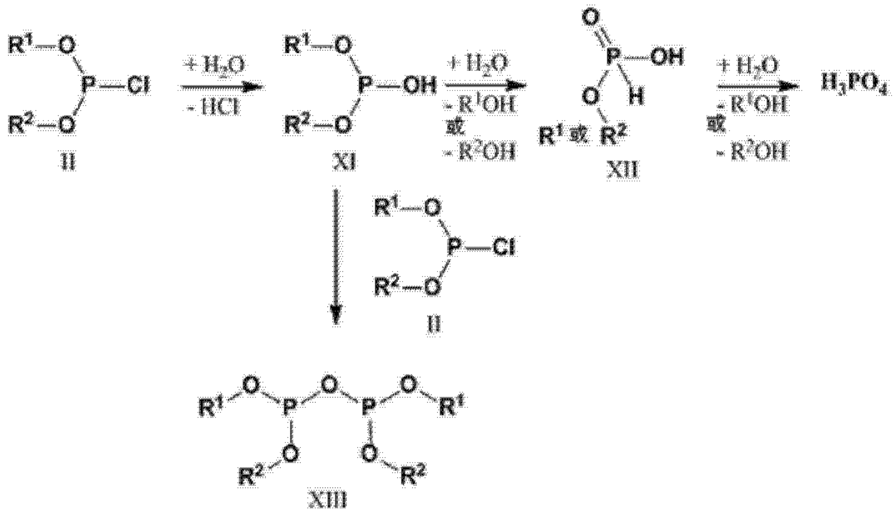
[0105]　单亚磷酸酯中间体（结构 X）的分子内反应产生各 1 当量的环亚磷酸酯和芳醇，即衍生自氯代亚磷酸酯的 $R^1$-OH 或 $R^2$-OH。在一些实例中，芳醇 $R^1$-OH 或 $R^2$-OH 还可以由如在本文中所描述的其他途径制备。取决于氯代亚磷酸酯的浓度，芳醇可以与另一当量的氯代亚磷酸酯反应以得到结构 IX 的无环亚磷酸三有机酯副产物，其在本文中被称为 T-phite 配体结构、或 TLS。单亚磷酸酯中间体的这种分子内反应因此可以造成联芳化合物和氯代亚磷酸酯二者转化为不希望的产物，作为 TLS 和 CLS 产生的结果，导致对 DLS 制备的较低选择性。在一些实例中，联芳化合物中、氯代亚磷酸酯中、或联芳化合物和氯代亚磷酸酯二者中较大量的空间体积可以引起较大比例的 TLS 和 CLS 产生和对 DLS 制备的较低选择性。

[0106]　氯代亚磷酸酯可以通过以下方式合成：$PCl_3$ 与芳醇 $R^1OH$ 和 $R^2OH$ 在适合的有机碱的存在下分步反应从而首先制备二氯代亚磷酸酯，例如 $(R^1O)PCl_2$，随后进一步反应以制备氯代亚磷酸酯，例如 $(R^1O)(R^2O)PCl$，其在本文中被表示为结构 II。例如，在 PCT 公开 WO2004/050588 中公开了结构 II 的氯代亚磷酸酯的合成。

[0107]　方案 II 示出了用于氯代亚磷酸酯的水解的总体反应方案。氯代亚磷酸酯可以与

水反应生成配体水解产物(LHP),其可以包括酸性含磷化合物(结构 XI 和 XII)、亚磷酸($H_3PO_3$)或其他含磷的酸,以及衍生自氯代亚磷酸酯的芳醇($R^1OH$ 或 $R^2OH$)。氯代亚磷酸酯还可以与初始水解产物(结构 XI)反应以形成含磷的酸酐(结构 XI)。

[0108]



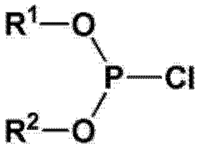
**方案 II**

[0109] 经验上,随着氯代亚磷酸酯转化率的增加,用于将单亚磷酸酯中间体(结构 X)转化为 CLS(结构 VI、VII、或 VIII)并且之后转化为 TLS(结构 IX)的分子内反应速率增加,并且至所需的 DLS(结构 I)的选择性降低。在高的氯代亚磷酸酯浓度下,与在更稀的反应条件下相比,用于将单亚磷酸酯中间体转化为 DLS 的速率增加。此外,稀溶液可以为氯代亚磷酸酯与任何存在的水污染反应以允许随后酸性含磷化合物的形成提供另外的机会,所述酸性含磷化合物可以充当形成 CLS 的不希望的分子内反应的催化剂。限制反应混合物中单亚磷酸酯中间体(结构 X)的浓度可以有助于实现对 DLS 形成的最大选择性。限制反应混合物中单亚磷酸酯中间体的浓度可以限制不希望的副产物如 TLS 或 CLS 的形成。

[0110] 接触

[0111] 本发明的多个实施方案包括,使结构 II 的氯代亚磷酸酯,

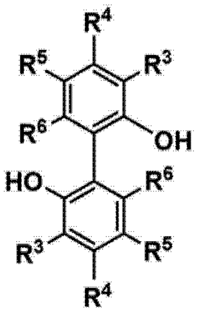
[0112]



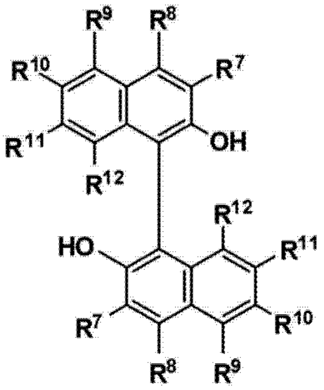
**结构 II**

[0113] 与选自由结构 III、结构 IV 和结构 V 组成的组的 X-OH 化合物(例如联芳化合物),

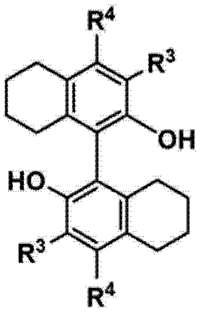
[0114]



结构 III



结构 IV



结构 V

[0115] 和有机叔胺接触以提供包含结构 I 的 DLS 的反应混合物。所述接触包括，在第一连续添加中将所述联芳化合物添加至所述氯代亚磷酸酯，以提供所述第一反应混合物。所述接触还包括，添加第二连续添加物，包括所述联芳化合物、水、或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇中的至少一种，以提供所述第二反应混合物。所述接触还可以包括添加第三添加物，或者所述第二反应混合物是最终反应混合物。在进行的情况下的所述第三添加可以包括，添加选自由所述联芳化合物、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供最终反应混合物。

[0116] 所述接触可以是任何适合的接触。在一个实例中，所述接触可以包括将任何适合的材料或适合的材料的混合物添加至任何其他适合的材料或适合的材料的混合物，并且可以以连续或间歇方式进行。一种或多种化合物向一种或多种其他化合物的添加可以在任何适合的时间段内进行；本领域技术人员将会容易地理解控制化学反应中添加速率的重要性，尤其是在大规模化学反应中。在一个实例中，接触可以包括将联芳化合物进料至氯代亚磷酸酯和有机叔胺的混合物中。在另一个实例中，接触可以包括将所述 X-OH 化合物（例如联芳化合物）和所述有机叔胺单独进料至所述氯代亚磷酸酯。在另一个实例中，接触可以包括将所述 X-OH 化合物（例如联芳化合物）和所述有机叔胺作为混合物进料至所述氯代亚磷酸酯。例如，接触可以包括将所述 X-OH 化合物（例如联芳化合物）连续或不连续地进料至包含氯代亚磷酸酯和有机叔胺的搅拌容器中。在另一个实例中，接触可以包括将所述 X-OH 化合物（例如联芳化合物）连续或不连续地进料至包含氯代亚磷酸酯和有机叔胺的混合物的连续流的管式反应器中。

[0117] 如以下进一步描述的，第一连续添加物包含 X-OH 和其他材料的添加。例如，所述第一连续添加可以包括联芳化合物，或联芳化合物和其他材料的混合物的添加。如以下进一步描述的，所述第二或第三连续添加也可以包括联芳化合物，或联芳化合物和其他材料的混合物的添加。然而，在一些实施方案中，第二或第三连续添加物不包含联芳化合物。

[0118] 在一些实施方案中，所述接触可以在充分混合的反应区中进行。适合的混合方法包括适合于反应容器的尺寸和形状的那些方法。混合方法的非限制性实例包括本领域技术人员已知的适合的方法如机械搅拌器、静态混合机、喷嘴、多孔管和降液管托盘。在一些实例中，可以使用液体分布器如喷嘴、多孔管、和降液管托盘来添加液体。在一些实例中，使液体（例如联芳溶液和有机叔胺）流过至少一个将液体引向位于上液面下面的叶轮的进料管线可以帮助确保液体与氯代亚磷酸酯在反应混合物的湍流混合区中的有效混合。在一些实

施方案中，联芳化合物或联芳溶液与氯代亚磷酸酯的不良混合可能导致联芳化合物和结构X的单亚磷酸酯中间体的局部高浓度，从而可能导致对DLS形成的选择性变差。

[0119] 在一些实例中，所述方法可以由氯代亚磷酸酯化合物以一定摩尔选择性制备在最终反应混合物中的含磷配体，使得最终反应混合物中作为含磷配体（例如DLS）的磷的总摩尔百分比为在约55％至约65％之间、或约65％至约75％之间、或约75％至约85％之间、或约85％至约90％之间、或约90％至约95％之间、或约95％至约100％之间。

[0120] 在一些实施方案中，所述方法可以包括，在例如其中氯代亚磷酸酯转化率为约0％至约90％的接触阶段期间，控制所述进料使得所述反应混合物中的氯代亚磷酸酯浓度大于或等于约0.02摩尔/升的平均分布。在一些实施方案中，在例如其中氯代亚磷酸酯转化率为约0％至约90％的接触阶段期间，所述反应混合物中的氯代亚磷酸酯浓度在约0.02摩尔/升至约2.0摩尔/升的平均分布之间。

[0121] 在多个方面中，所述方法可以包括，以相对于通过所述方法进行所述接触的氯代亚磷酸酯的总摩尔数在约0.04至约10摩尔当量/小时之间的进料速率，将联芳化合物进料至所述氯代亚磷酸酯。例如，以在约0.5至约10摩尔当量/小时之间的进料速率，将联芳化合物进料至氯代亚磷酸酯。

[0122] 在一些实例中，所述第一反应混合物具有化学计量过量的氯代亚磷酸酯。在一些实例中，所述第二反应混合物具有化学计量过量的氯代亚磷酸酯。

[0123] 在一些实施方案中，水可能对DLS形成的选择性有害。在一些实例中，可以将水经由任何进料流引入至所述反应混合物中，例如利用联芳化合物、有机叔胺、或联芳化合物和有机叔胺的组合。在实例中，在与氯代亚磷酸酯接触之前，可以通过相分离、蒸馏、共沸蒸馏、与干燥分子筛接触、干燥柱和本领域中已知的其它适合的方法将水至少部分地与联芳化合物和有机叔胺分离。

[0124] 在本发明的一个实施方案中，第一连续添加物可以包含足够量的所述X-OH化合物（例如联芳化合物），使得第一反应混合物中所述氯代亚磷酸酯的转化率为约85％至约95％；所述第二连续添加物可以包含比在所述第一连续添加中添加的所述X-OH化合物的量更小的量的所述X-OH化合物。

[0125] 在本发明的另一个实施方案中，第一连续添加物可以包含足够量的所述X-OH化合物，使得第一反应混合物中所述氯代亚磷酸酯的转化率为约85％至约91％；所述第二连续添加物可以包含足够量的具有化学结构$R^1$-OH或$R^2$-OH的醇，使得在所述第二（例如最终）反应混合物中剩余的氯代亚磷酸酯转化为适合的副产物（例如所述TLS）。在一些实例中，所述第二连续添加物可以包含足够量的具有化学结构$R^1$-OH或$R^2$-OH的醇，使得在所述第二反应混合物中氯代亚磷酸酯转化率为约100％。

[0126] 如将会容易地由本领域技术人员理解的，因为反应物逐渐转化为产物并且实现在其中反应产物达到相对稳定浓度的近似平衡状态，第一、第二、和最终反应混合物可以具有随时间演变的组成。达到近似平衡状态的时间量可以为，例如，1秒至约10天、约1分钟至约5天、或约10分钟至约1天、或约1小时至约10小时。在另一个实例中，达到近似平衡状态的时间可以为，例如，约1秒至约1分钟、或约1分钟至约1小时、约1小时至约5小时、或约5小时至约24小时。一般而言，当在本文中提及第一、第二、或最终反应混合物的组成时，除非另外指出，参照在产生反应混合物的特定的添加步骤已经完成（例如第一添加、第

二添加、或第三添加（如果进行）），反应已经基本上进行完全，并且已经达到近似平衡状态之后的第一反应混合物的组成。

[0127] 所述接触还包括，确定作为至少一种副产物存在于所述第一反应混合物中的磷的摩尔百分比。所述接触还包括，利用作为所述至少一种副产物存在于所述第一反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第二连续添加中添加的选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量。在这种确定中的至少一种副产物可以是，例如，CLS、TLS、LHP、氯代亚磷酸酯、任何适合的副产物、或它们的任何组合。

[0128] 烃溶剂

[0129] 在一些实施方案中，反应混合物可以包含至少一种芳族烃溶剂。烃溶剂可以包括任何适合的烃溶剂。芳族烃溶剂可以选自由 $C_6$ 至 $C_{18}$ 芳族烃组成的组。在一些实施方案中，所述方法可以包括，将所述 X-OH 化合物以包含所述 X-OH 化合物和烃溶剂的所述 X-OH 化合物的溶液形式进料至所述氯代亚磷酸酯。在一些实例中，烃溶剂可以是选自由以下各项组成的组的烃：直链非环状 $C_5$ 至 $C_{18}$ 脂族烃、支链非环状 $C_5$ 至 $C_{18}$ 脂族烃、未取代的环状 $C_5$ 至 $C_{18}$ 脂族烃、取代的环状 $C_5$ 至 $C_{18}$ 脂族烃、未取代的 $C_6$ 至 $C_{10}$ 芳族烃、和 $C_6$ 至 $C_{18}$ 取代的芳族烃。烃溶剂可以选自由其在大气压下的沸点介于 70℃至 145℃之间的烃组成的组。适合的芳族烃溶剂的实例包括 $C_{1-5}$ 取代的苯、$C_{1-5}$ 取代的苯酚、和任何适合的取代形式的二甲苯或二甲苯酚。适合的芳族烃溶剂的具体实例包括甲苯。在一些实例中，将 X-OH 化合物以包含 X-OH 化合物和烃溶剂的溶液形式进料至氯代亚磷酸酯。

[0130] 接触的温度

[0131] 接触的温度可以是任何适合的温度。在一些实施方案中，所述接触可以在表 1 的左栏中所列的温度范围内的温度下进行。在其它实施方案中，所述方法中的所述接触可以在表 1 的右栏中所列的温度范围内的温度下进行。在本发明的其它方面中，反应混合物包含烃溶剂，并且表 1 的右栏中反应混合物在 1 个大气压（1atm）的沸点约等于烃溶剂的沸点。在多个实施方案中，可以将烃溶剂与氯代亚磷酸酯、X-OH 化合物（例如联芳化合物）、有机叔胺，与这些成员的任何组合，或与这些反应物相独立地引入至反应混合物中。

[0132] 表 1. 在多个实施方案中用于接触步骤的适合的温度范围

[0133]

| 温度范围 | 温度范围 |
|---|---|
| 约 10 至约 110℃ | 约 10℃至混合物在 1atm 下的沸点 |
| 约 15 至约 110℃ | 约 15℃至混合物在 1atm 下的沸点 |
| 约 20 至约 110℃ | 约 20℃至混合物在 1atm 下的沸点 |
| 约 25 至约 110℃ | 约 25℃至混合物在 1atm 下的沸点 |
| 约 30 至约 110℃ | 约 30℃至混合物在 1atm 下的沸点 |
| 约 35 至约 110℃ | 约 35℃至混合物在 1atm 下的沸点 |

| | |
|---|---|
| 约 40 至约 110℃ | 约 40℃至混合物在 1atm 下的沸点 |
| 约 45 至约 110℃ | 约 45℃至混合物在 1atm 下的沸点 |
| 约 50 至约 110℃ | 约 50℃至混合物在 1atm 下的沸点 |
| 约 55 至约 110℃ | 约 55℃至混合物在 1atm 下的沸点 |
| 约 60 至约 110℃ | 约 60℃至混合物在 1atm 下的沸点 |

[0134] 有机叔胺

[0135] 有机叔胺可以是任何适合的有机叔胺，并且可以以任何适合的量添加。在一些实施方案中，有机叔胺可以以足以中和反应混合物中 HCl 副产物的量添加。胺可以加速反应速率并且可以限制可能会降低 DLS 形成的选择性的酸催化化学反应。在一些实例中，所述方法包括在所述接触步骤期间使有机叔胺盐酸盐从所述反应混合物中沉淀。在一些实例中，有机叔胺的选择和在烃溶剂的存在下的接触二者都能够使有机叔胺盐酸盐从反应混合物沉淀出来。

[0136] 包含单个碱性氮原子的适合的有机叔胺的实例可以是 (R’)(R”)(R”’)N 化合物，其中 R’、R”、和 R”’ 独立地选自由 $C_1$ 至 $C_{10}$ 烷基和 $C_6$ 至 $C_{10}$ 芳基组成的组，可以是芳族叔胺化合物，例如吡啶，或者可以是包含单个碱性氮原子的有机叔胺的组合。适合的胺的一个实例包括具有独立地选择的烷基并且具有 1 至 10 个碳原子的三烷基胺，如三乙胺。其他实例包括，包含多个的碱性氮原子、具有无 N-H 键的氮原子的有机叔胺；例如 N，N，N’，N’－四甲基乙二胺。在一些实例中，第一添加、第二添加、第三添加（如果进行）、或它们的任何组合可以在化学计量过量的有机叔胺的存在下进行。

[0137] 组分的重量百分比范围

[0138] 在本文中提供了多种反应物的摩尔范围的其他实例，在本章节中提供的范围是非限制性的实例。

[0139] 在一些实例中，氯代亚磷酸酯可以为在全部第一、第二、和第三添加（如果进行）中添加的氯代亚磷酸酯、联芳化合物、和有机叔胺的总量的约 10 重量％至约 90 重量％、约 20 重量％至约 80 重量％、或约 30 重量％至约 70 重量％。在一些实施方案中，氯代亚磷酸酯可以为添加的氯代亚磷酸酯、联芳化合物、和有机叔胺的总量的约 40 重量％至约 60 重量％、约 45 重量％至约 55 重量％、或约 48 重量％至约 52 重量％。

[0140] 在一些实例中，联芳化合物可以为在全部第一、第二、和第三添加（如果进行）中添加的氯代亚磷酸酯、联芳化合物、和有机叔胺的总量的约 1 重量％至约 80 重量％、约 5 重量％至约 70 重量％、或约 10 重量％至约 60 重量％。在一些实施方案中，联芳化合物可以为添加的氯代亚磷酸酯、联芳化合物、和有机叔胺的总量的约 10 重量％至约 45 重量％、约 20 重量％至约 35 重量％、或约 25 重量％至约 30 重量％。

[0141] 在一些实例中，有机叔胺可以为在全部第一、第二、和第三添加（如果进行）中添加的氯代亚磷酸酯、联芳化合物、和有机叔胺的总量的约 1 重量％至约 99 重量％、约 5 重量％至约 70 重量％、或约 10 重量％至约 60 重量％。在一些实施方案中，有机叔胺可以为添加的氯代亚磷酸酯、联芳化合物、和有机叔胺的总量的约 5 重量％至约 40 重量％、约 15

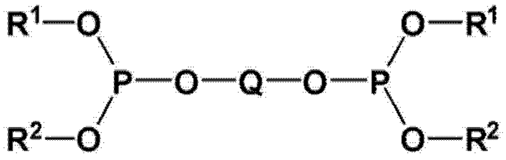
重量%至约 30 重量%、或约 20 重量%至约 25 重量%。

[0142] 在一些实例中，芳族烃溶剂可以以下列量存在：在全部第一、第二、和第三添加（如果进行）中添加的芳族烃溶剂、氯代亚磷酸酯、联芳化合物、和有机叔胺的总量的约 1 重量%至约 99.999 重量%、约 5 重量%至约 80 重量%、或约 10 重量%至约 60 重量%。在一些实施方案中，芳族烃溶剂可以以下列量存在：添加的芳族烃溶剂、氯代亚磷酸酯、联芳化合物、和有机叔胺的总量的约 5 重量%至约 70 重量%、约 15 重量%至约 50 重量%、或约 25 重量%至约 40 重量%。

[0143] D-phite 配体结构 (DLS)

[0144] 如以上所描述的，在具体实施方案中，本发明的方法可以制备具有结构 I 的化学结构的二亚磷酸酯配体结构 (DLS)，

[0145]

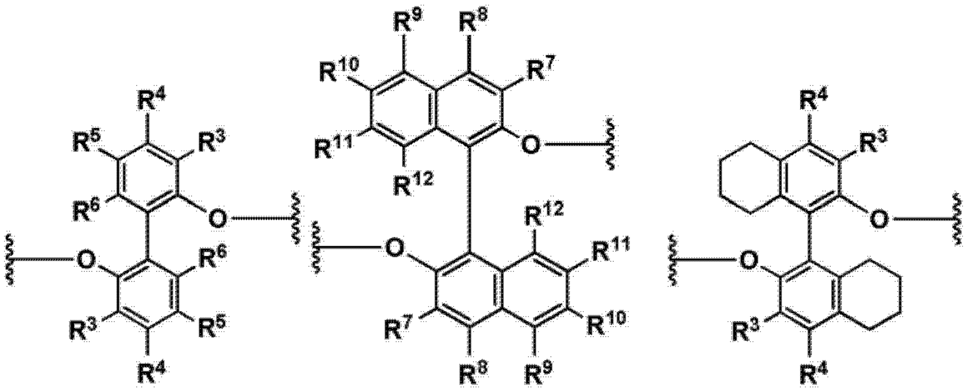


结构 I。

[0146] 在结构 I 中，$R^1$ 和 $R^2$ 可以是相同或不同的、取代或未取代的单价芳基。在一些实例中，$R^1$ 和 $R^2$ 可以是取代的或未取代的芳基。在一些实例中，$R^1$ 和 $R^2$ 可以是 $C_{1-10}$ 烷基取代的苯基。在一些实例中，$R^1$ 和 $R^2$ 可以是相同的。在一些实例中，$R^1$ 和 $R^2$ 可以是二甲苯基（例如单价二甲苯基团），例如 2,4- 二甲苯基。

[0147] 在结构 I 中，O-Q-O 是具有结构 III、IV、和 V 的联芳化合物的二价物种。因此，O-Q-O 可以由以下三种结构中的一个表示：

[0148]

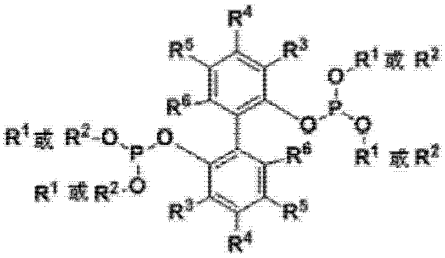


[0149] 其中 $R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和 $R^{12}$ 中的每一个可以是任何适合的官能团。在一个实例中，$R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和 $R^{12}$ 独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团。在一个实例中，$R^3$ 至 $R^{12}$ 可以是直链、支链、和环状 $C_1$ 至 $C_{18}$ 烷基；取代的或未取代的 $C_6$ 至 $C_{18}$ 芳基；取代的或未取代的 $C_6$ 至 $C_{18}$ 芳氧基；直链、支链、和环状 $C_1$ 至 $C_{18}$ 烷氧基；直链和支链 $C_2$ 至 $C_{18}$ 烷氧基烷基；取代的或未取代的 $C_3$ 至 $C_{18}$ 环状缩醛；取代的或未取代的 $C_7$ 至 $C_{18}$ 芳氧羰基；直链、支

链、和环状 $C_2$ 至 $C_{18}$ 烷氧羰基；取代的或未取代的 $C_7$ 至 $C_{18}$ 芳基羰基；和取代的或未取代的 $C_2$ 至 $C_{18}$ 烷基羰基。

[0150] 在一些实施方案中，DLS 可以由以下结构表示：

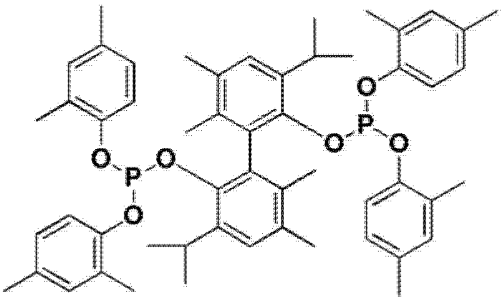
[0151]



[0152] 其中 $R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

[0153] 在一些实施方案中，DLS 可以由以下结构表示：

[0154]



。

[0155] 因此，$R^1$ 和 $R^2$ 可以是 2,4- 二甲苯基，$R^3$ 可以是异丙基，$R^4$ 可以是氢，并且 $R^5$ 和 $R^6$ 可以是甲基。在一些实施方案中，可以在 $^{31}P$ NMR 光谱中通过在约 131.8ppm 出现的峰鉴别 DLS 化合物，如在本段中描述的化合物。

[0156] 在一些实施方案中，在最终反应混合物中，作为含磷配体结构存在的磷的百分比可以为约 1％至约 100％或约 30％至约 100％、或约 50％至约 99％、或约 55％至约 95％、或约 60％至约 90％、或约 60％至约 80％、或约 62％至约 85％、或约 64％至约 80％、或约 65％、或约 70％。

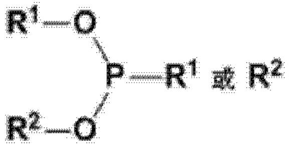
[0157] 在一些实施方案中，在所述最终反应混合物中，作为所述含磷配体结构存在的磷的百分比大于或等于约 65％，并且作为所述 LHP 存在的磷的百分比小于不大于约 5％。在一些实施方案中，在所述最终反应混合物中，作为所述含磷配体结构存在的磷的百分比大于或等于约 70％，并且作为所述 LHP 存在的磷的百分比小于不大于约 3.5％。在一些实施方案中，在所述最终反应混合物中，作为所述含磷配体结构存在的磷的百分比大于或等于约 65％，并且作为所述 CLS 存在的磷的百分比小于约 5％。在一些实施方案中，在所述最终反应混合物中，作为所述含磷配体结构存在的磷的百分比大于或等于约 70％，并且作为所述 CLS 存在的磷的百分比小于约 3.5％。

[0158] T-phite 配体结构 (TLS) 和 C-phite 配体结构 (CLS)

[0159] 如以上方案 I 中所述的，在一些实施方案中，所述方法可以在最终反应混合物中产生至少一种含磷副产物，所述含磷副产物选自由以下各项组成的组：$P(OR^1)(OR^2)_2$、$P(OR^1)_2(OR^2)$、$P(OR^1)_3$（当 $R^2 = R^1$ 时）、$P(OR^2)_3$（当 $R^1 = R^2$ 时）、以下作为结构 IX 所示的

TLS 结构：

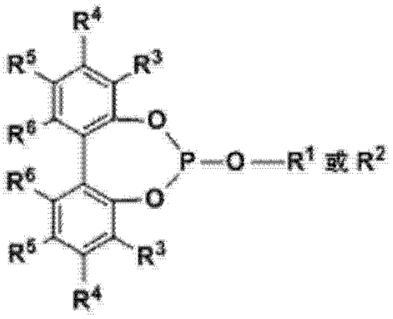
[0160]



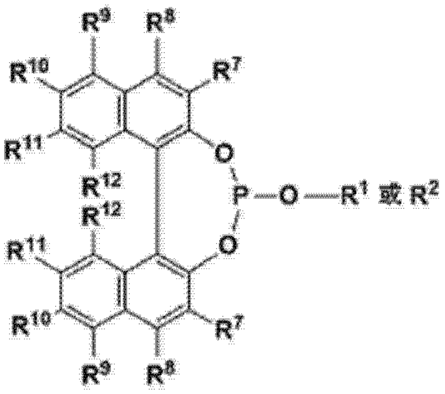
结构 IX、

[0161] 以及以下所示的 CLS 结构 VI、VII、或 VIII 的化合物：

[0162]

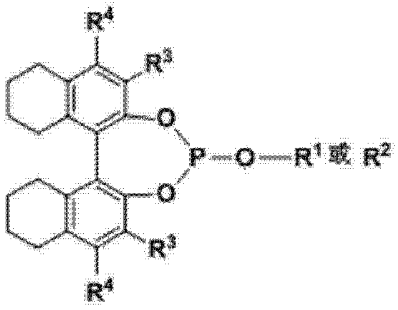


结构 VI



结构 VII

[0163]



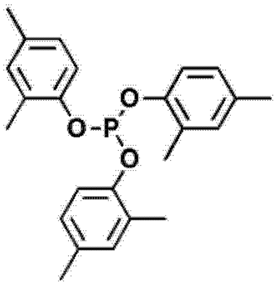
结构 VIII。

[0164] 在以上给出的 TLS 和 CLS 结构中，$R^1$ 和 $R^2$ 可以是相同或不同的、取代或未取代的单价芳基。在一些实例中，$R^1$ 和 $R^2$ 可以是取代的或未取代的芳基。在一些实例中，$R^1$ 和 $R^2$ 可以是 $C_{1-10}$ 烷基取代的苯基。在一些实例中，$R^1$ 和 $R^2$ 可以是相同的。在一些实例中，$R^1$ 和 $R^2$ 可以是二甲苯基（例如单价二甲苯基团），例如 2，4- 二甲苯基。$R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和 $R^{12}$ 中的每一个可以是任何适合的官能团。在一个实例中，$R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和 $R^{12}$ 独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、噁唑基、胺基、酰胺基、

腈基、巯基、和卤素基团。在一个实例中，$R^3$ 至 $R^{12}$ 可以是直链、支链、和环状 $C_1$ 至 $C_{18}$ 烷基；取代的或未取代的 $C_6$ 至 $C_{18}$ 芳基；取代的或未取代的 $C_6$ 至 $C_{18}$ 芳氧基；直链、支链、和环状 $C_1$ 至 $C_{18}$ 烷氧基；直链和支链 $C_2$ 至 $C_{18}$ 烷氧基烷基；取代的或未取代的 $C_3$ 至 $C_{18}$ 环状缩醛；取代的或未取代的 $C_7$ 至 $C_{18}$ 芳氧羰基；直链、支链、和环状 $C_2$ 至 $C_{18}$ 烷氧羰基；取代的或未取代的 $C_7$ 至 $C_{18}$ 芳基羰基；和取代的或未取代的 $C_2$ 至 $C_{18}$ 烷基羰基。

[0165] 在一些实施方案中，TLS 可以由以下结构表示：

[0166]

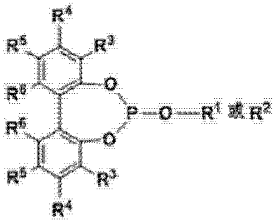


。

[0167] 因此，$R^1$ 或 $R^2$ 可以是 2,4- 二甲苯基。在一些实施方案中，可以在 $^{31}$PNMR 光谱中通过在约 131.2ppm 出现的峰鉴别 TLS 化合物，如在本段中描述的化合物。

[0168] 在一些实施方案中，CLS 可以由以下结构表示：

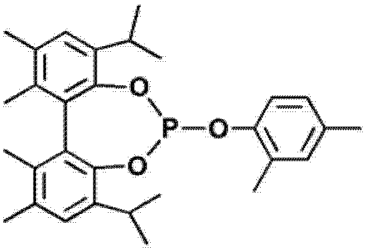
[0169]



[0170] 其中 $R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

[0171] 在一些实施方案中，CLS 可以由以下结构表示：

[0172]



。

[0173] 因此，$R^1$ 或 $R^2$ 可以是 2,4- 二甲苯基，$R^3$ 可以是异丙基，$R^4$ 可以是氢，并且 $R^5$ 和 $R^6$ 可以是甲基。在一些实施方案中，可以在 $^{31}$P NMR 光谱中通过在约 136.0ppm 出现的峰鉴别 CLS 化合物，如在本段中描述的化合物。

[0174] 预定极限值

[0175] 在多个实例中，所述接触包括，为反应混合物中作为特定产物，例如在最终反应混合物中作为特定的副产物存在的磷的百分比规定预定极限值。预定极限值可以是任何适合的预定极限值。可以在任何适合的时间规定预定极限值，如例如在第一添加之前、在第二添

加之前、或在第三添加之前(如果进行)。在一个实例中,反应混合物中作为特定产物存在的磷的百分比是摩尔百分比。在另一个实例中,反应混合物中作为特定产物存在的磷的百分比可以基于质量或基于任何其他适合的量度。预定极限值可以基于反应混合物中的全部含磷化合物。在一个实例中,预定极限值可以是最终反应混合物中作为特定产物存在的磷的百分比的希望的规格极限值。在另一个实例中,预定极限值可以是低于最终反应混合物中作为特定产物存在的磷的百分比的希望的规格极限值的一些数值。通过选择低于规格极限值的预定极限值,这样可以有助于确保在最终产物混合物中实现实际的规格极限值,并且可以允许一定幅度的误差。然而,在一些实施方案中,采用无误差幅度,并且预定极限值对应于最终反应混合物中作为特定产物存在的磷的百分比的希望的规格极限值。

[0176] 在一些实例中,所述接触包括,为所述最终反应混合物中作为 CLS 存在的磷的摩尔百分比规定预定极限值。所述最终反应混合物中作为 CLS 存在的磷的摩尔百分比预定极限值可以是任何适合的预定极限值。在一个实例中,所述最终反应混合物中作为 CLS 存在的磷的摩尔百分比预定极限值为约 0 摩尔%至约 99 摩尔%、约 0 摩尔%至约 50 摩尔%、或约 0 摩尔%至约 5 摩尔%。在另一个实例中,所述最终反应混合物中作为 CLS 存在的磷的摩尔百分比预定极限值为约 0 摩尔%至约 16 摩尔%、约 1 摩尔%至约 8 摩尔%、或约 2 摩尔%至约 4 摩尔%。在另一个实例中,所述最终反应混合物中作为 CLS 存在的磷的摩尔百分比预定极限值为约 0 摩尔%至约 6 摩尔%、约 0 摩尔%至约 4 摩尔%、或约 0 摩尔%至约 2 摩尔%。在本段中给出的任何预定极限值也可以是所述最终反应混合物中作为所述 CLS 存在的磷的百分比的实例。

[0177] 在一些实例中,所述接触包括,为所述最终反应混合物中作为 TLS 存在的磷的摩尔百分比规定预定极限值。所述最终反应混合物中作为 TLS 存在的磷的摩尔百分比预定极限值可以是任何适合的预定极限值。在一个实例中,所述最终反应混合物中作为 TLS 存在的磷的摩尔百分比预定极限值为约 0 摩尔%至约 100 摩尔%、或约 0 摩尔%至约 50 摩尔%。在另一个实例中,所述最终反应混合物中作为 TLS 存在的磷的摩尔百分比预定极限值为约 2 摩尔%至约 50 摩尔%、约 5 摩尔%至约 40 摩尔%、或约 10 摩尔%至约 30 摩尔%。在另一个实例中,所述最终反应混合物中作为 TLS 存在的磷的摩尔百分比预定极限值为约 3 摩尔%至约 80 摩尔%、约 7 摩尔%至约 40 摩尔%、或约 14 摩尔%至约 21 摩尔%。在本段中给出的任何预定极限值也可以是所述最终反应混合物中作为所述 TLS 存在的磷的百分比的实例。

[0178] 在一个实例中,所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比预定极限值为约 0 摩尔%至约 99 摩尔%、约 0 摩尔%至约 50 摩尔%、或约 0 摩尔%至约 5 摩尔%。所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比预定极限值可以是任何适合的预定极限值。在另一个实例中,所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比预定极限值为约 0 摩尔%至约 16 摩尔%、约 1 摩尔%至约 8 摩尔%、或约 2 摩尔%至约 4 摩尔%。在另一个实例中,所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比预定极限值为约 0 摩尔%至约 6 摩尔%、约 0 摩尔%至约 4 摩尔%、或约 0 摩尔%至约 2 摩尔%。在本段中给出的任何预定极限值也可以是所述最终反应混合物中作为所述 LHP 存在的磷的百分比的实例。

[0179] 规定预定极限值可以包括,为所述最终反应混合物中作为 TLS、CLS、LHP、DLS、任何

其他适合的副产物中的一种或多种存在的磷的百分比规定预定极限值。

[0180] 百分比转化率

[0181] 在一些实施方案中，可以进行关于第一连续添加物的组成的确定，包括利用第一反应混合物中所述氯代亚磷酸酯的转化率的预定目标值。因此，接触可以包括，为所述第一反应混合物中氯代亚磷酸酯的转化率规定预定目标值。可以在添加第一添加物之前为所述第一反应混合物中氯代亚磷酸酯的转化率规定预定目标值。接触还可以包括，利用所述第一反应混合物中氯代亚磷酸酯的所述转化率的预定目标值来确定在所述第一连续添加中添加的联芳化合物的量。例如，可以利用所述第一反应混合物中氯代亚磷酸酯的所述转化率的预定目标值来确定在所述第一连续添加中添加的联芳化合物的量，使得所述第一反应混合物中所述氯代亚磷酸酯的所述百分比转化率等于或高于所述预定目标值。

[0182] 所述第一反应混合物中所述氯代亚磷酸酯的转化率的预定目标值可以是任何适合的预定目标值。在一些实施方案中，所述第一反应混合物中所述氯代亚磷酸酯的转化率的预定目标值为约30％至约100％、或约70％至约100％、或约80％至约97％、或约85％至约95％、或约88％至约92％、或约90％。

[0183] 在一些实施方案中，可以进行关于第二连续添加物的组成的确定，包括利用第二反应混合物中氯代亚磷酸酯的转化率的预定目标值。因此，接触可以包括，为所述第二反应混合物中氯代亚磷酸酯的转化率规定预定目标值。在一些实施方案中，可以在添加第一连续添加物之前进行所述第二反应混合物中氯代亚磷酸酯的所述转化率的预定目标值的规定。在其它实施方案中，可以在添加第一连续添加物之前为所述第二反应混合物中氯代亚磷酸酯的转化率规定预定目标值。接触还可以包括，在添加第一连续添加物之后，确定所述第一反应混合物中所述氯代亚磷酸酯的所述转化率。接触还可以包括，在添加所述第二连续添加物之前，利用所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值的比较，来确定要在所述第二连续添加中添加的特定化合物的量。例如，接触可以包括，利用所述第一反应混合物中所述氯代亚磷酸酯的转化率与所述第二反应混合物中所述氯代亚磷酸酯的转化率的预定目标值的比较，来确定要在所述第二连续添加中添加的选自由所述X-OH、水、或所述具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物的量，使得所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率等于或高于预定目标值。

[0184] 所述第二反应混合物中所述氯代亚磷酸酯的转化率的预定目标值可以是任何适合的预定目标值。在一些实施方案中，所述第二反应混合物中氯代亚磷酸酯的所述转化率的预定目标值为约50％至约100％、或约70％至约100％、或约90％至约99％、或约95％至约99％、或约98％。

[0185] 在一些实施方案中，所述第二反应混合物中氯代亚磷酸酯的所述转化率的预定目标值为约80％至约100％。在一些实例中，所述第二反应混合物中氯代亚磷酸酯的所述转化率的预定目标值为约96％至约99％。在一些实例中，所述第一反应混合物中氯代亚磷酸酯的所述转化率的预定目标值为约85％至约95％。在一些实例中，所述第一反应混合物中氯代亚磷酸酯的所述转化率的预定目标值为约90％。

[0186] 配体水解产物(LHP)

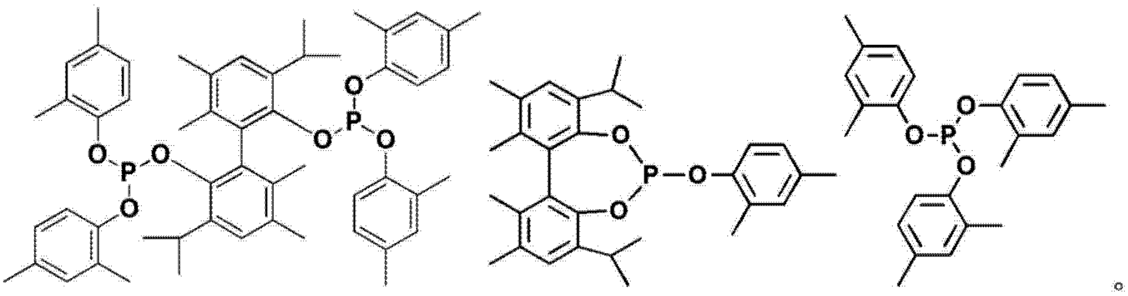
[0187] 在一些实施方案中，可以进行关于第二连续添加物的组成的确定，包括利用所述

最终反应混合物中作为LHP存在的磷的摩尔百分比的预定极限值。

[0188] 在一些实施方案中，配体水解产物可以是存在于反应混合物中的任何材料的任何适合的水解产物。当在本文中讨论LHP时，LHP的任何适合的量可以被提及，包含一些或全部LHP。LHP可以包含通过包括以下各项的过程得到的产物：所述含磷配体或所述氯代亚磷酸酯的水解。LHP可以包含通过包括以下各项的过程得到的产物：衍生自所述含磷配体或衍生自所述氯代亚磷酸酯的产物的水解。LHP可以包含通过包括以下各项的过程得到的产物：所述含磷配体的水解产物或所述氯代亚磷酸酯的水解产物的反应，或衍生自所述含磷配体或衍生自所述氯代亚磷酸酯的产物的水解产物的反应。LHP可以包含DLS、TLS、CLS、或氯代亚磷酸酯的任何水解产物，其中在其中的任何一个P-OR键和在其中的任何多个P-OR键都被P-OH键代替。LHP还可以包含衍生自配体水解产物的材料，如例如酸酐，其通过例如两个P-OR键形成P-O-P结构的反应而形成。

[0189] 在一些实施方案中，LHP化合物可以衍生自以下所示的结构：

[0190]



[0191] 在一些实施方案中，可以利用$^{31}$P NMR通过在约30ppm至约-20ppm出现的峰来鉴别LHP化合物，如在本段中描述的那些化合物。

[0192] 确定摩尔百分比和转化率

[0193] 所述接触可以包括，确定作为副产物存在于所述第一或第二反应混合物中的磷的摩尔百分比。例如，所述接触可以包括，确定CLS、TLS、LHP、或任何其他适合的副产物的所述第一或第二反应混合物中存在的磷的摩尔百分比。在一些实施方案中，确定作为一种或多种特定副产物存在于所述第一或第二反应混合物中的磷的摩尔百分比可以包括，抽取样品以分析液体反应混合物，例如通过$^{31}$P NMR、$^{1}$H NMR、液相或气相色谱法、质谱法、红外或UV光谱法、或它们的任何组合分析。所抽取的样品可以是任何适合的量，并且所使用的分析方法可以是任何适合的分析方法。

[0194] 例如，使用在本领域内众所周知的NMR分析技术，可以使用对应于特定化合物的NMR峰的积分来计算反应混合物中多种化合物的摩尔比，例如基于积分比和摩尔比之间的比例。基于对在最后添加之前添加的和/或已经存在于混合物中的试剂的总量的了解，可以使用摩尔比来确定反应混合物中作为特定产物存在的磷的摩尔百分比。

[0195] 第一连续添加

[0196] 所述接触包括，在第一连续添加中将所述X-OH化合物添加至所述氯代亚磷酸酯，以提供所述第一反应混合物。可以在第一连续添加中将任何适合量的X-OH化合物添加至任何适合量的氯代亚磷酸酯，并且所述添加可以以任何适合的速率进行。第一连续添加可以在任何适合的温度下进行。在一个实例中，X-OH化合物可以是联芳化合物。

[0197] 在一些实例中，所述接触可以包括利用所述最终反应混合物中作为至少一种副产

物存在的磷的摩尔百分比的预定极限值来确定在所述第一连续添加中添加的所述 X-OH 的量，以使作为所述至少一种副产物存在于所述第一反应混合物中的磷的摩尔百分比小于所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值。

[0198] 在一些实施方案中，在所述第二连续添加中添加的所述 X-OH 的量可以小于在所述第一连续添加中添加的所述 X-OH 的量。

[0199] 在一些实例中，所述接触包括，为所述第一反应混合物中氯代亚磷酸酯的转化率规定预定目标值。所述接触还可以包括，在添加第一连续添加物之前，利用所述第一反应混合物中氯代亚磷酸酯的所述转化率的预定目标值来确定在所述第一连续添加中添加的所述 X-OH 的量，使得所述第一反应混合物中氯代亚磷酸酯的转化率等于或高于所述第一反应混合物中氯代亚磷酸酯的转化率的预定目标值。

[0200] 在多个实施方案中，所述第一反应混合物可以具有化学计量过量的氯代亚磷酸酯。

[0201] 第二连续添加

[0202] 所述接触还包括，向所述第二反应混合物添加所述第二连续添加物，包括所述 X-OH 化合物、水、或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇中的至少一种，以提供所述第二反应混合物。可以在第二连续添加中将任何适合量的 X-OH 化合物、水、或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇中的至少一种添加至第一反应混合物，并且所述添加可以以任何适合的速率进行。第二连续添加可以在任何适合的温度下进行。在一个实例中，X-OH 化合物可以是联芳化合物。在其中不进行第三添加步骤的实施方案中，第二反应混合物是最终反应混合物。在其中进行第三添加步骤的实施方案中，第二反应混合物不是最终反应混合物。

[0203] 在一些实施方案中，所述接触可以包括，利用所述最终反应混合物中作为至少一种副产物存在的磷的摩尔百分比的预定极限值来确定在所述第一或第二连续添加中添加的所述 X-OH 的量，以使作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比小于所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值。

[0204] 在一些实例中，在所述第二连续添加中添加的所述 X-OH 的量为零。

[0205] 在一些实施方案中，如果在所述第二连续添加中添加的所述 X-OH 的量为零，则所述第二连续添加物包含水或具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇中的至少一种。

[0206] 在一些实施方案中，利用作为所述 CLS 存在于所述第一反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值的比较确定要在所述第二连续添加中添加的化合物的量，包括在所述第二添加中添加一定量的选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，所述一定量足以使作为所述 CLS 存在于所述第二反应混合物中的磷的摩尔百分比等于或低于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值。在一些实例中，如果作为所述 CLS 存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含水或具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。在一些实例中，如果作为所述 CLS 存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含所述 X-OH。

[0207] 在一些实施方案中，利用作为所述TLS存在于所述第一反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值的比较确定要在所述第二连续添加中添加的化合物的量，包括在所述第二添加中添加一定量的选自由所述X-OH、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，所述一定量足以使作为所述TLS存在于所述第二反应混合物中的磷的摩尔百分比等于或低于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值。在一些实例中，如果作为所述TLS存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含水。在一些实例中，如果作为TLS存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含所述X-OH或所述具有化学结构$R^1$-OH或$R^2$-OH的醇。

[0208] 在一些实施方案中，利用作为所述LHP存在于所述第一反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述LHP存在的磷的摩尔百分比的预定极限值的比较确定要在所述第二连续添加中添加的化合物的量，包括在所述第二添加中添加一定量的选自由所述X-OH、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，所述一定量足以使作为所述LHP存在于所述第二反应混合物中的磷的摩尔百分比等于或低于所述最终反应混合物中作为所述LHP存在的磷的摩尔百分比的预定极限值。在一些实例中，如果作为LHP存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述LHP存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含所述X-OH或所述具有化学结构$R^1$-OH或$R^2$-OH的醇。在一些实例中，如果作为LHP存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述LHP存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含水。

[0209] 在一些实例中，如果在所述第一反应混合物中作为所述CLS和所述TLS存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比的相应预定极限值，则所述第二连续添加物包含水。在一些实例中，如果在所述第一反应混合物中作为所述CLS和所述TLS存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比的相应预定极限值，则所述第二连续添加物不包含所述X-OH或所述具有化学结构$R^1$-OH或$R^2$-OH的醇。

[0210] 在一些实例中，所述接触包括，为所述第二反应混合物中氯代亚磷酸酯的转化率规定预定目标值。所述接触还可以包括，在添加第一连续添加物之后，确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率。并且，所述接触还可以包括，在添加所述第二连续添加物之前，利用所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的所述转化率的预定目标值的比较，来确定要在所述第二连续添加中添加的所述X-OH的量。

[0211] 在一些实施方案中，所述接触包括，为所述第二反应混合物中氯代亚磷酸酯的转化率规定预定目标值。所述接触还可以包括，在添加第一连续添加物之后，确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率。所述接触还可以包括，在添加所述第二连续添加物之前，利用所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的所述转化率的预定目标值的比较，来确定要在所述第二连续

添加中添加的所述 X-OH 的量。在一些实例中，如果在所述第一反应混合物中作为所述 CLS 或作为所述 TLS 存在的磷的摩尔百分比都不等于或不高于所述最终反应混合物中作为所述 CLS 或作为所述 TLS 存在的磷的摩尔百分比的相应预定极限值，并且所述第一反应混合物中氯代亚磷酸酯的所述转化率小于所述最终反应混合物中氯代亚磷酸酯的所述转化率的预定目标值，则要在所述第二连续添加中添加的所述 X-OH 的量足以使所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率等于或高于所述第二反应混合物中所述氯代亚磷酸酯的所述转化率的预定目标值。在一些实例中，如果在所述第一反应混合物中作为所述 CLS 或作为所述 TLS 存在的磷的摩尔百分比都不等于或不高于所述最终反应混合物中作为所述 CLS 或作为所述 TLS 存在的磷的摩尔百分比的相应预定极限值，并且所述第一反应混合物中氯代亚磷酸酯的所述转化率小于第二反应混合物中氯代亚磷酸酯的所述转化率的预定目标值，则所述第二连续添加物不包含水或具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。

[0212] 在一些实施方案中，接触可以包括，为所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比规定预定极限值。接触还可以包括，在添加第一连续添加物之后，确定所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比。所述接触还可以包括，在添加所述第二连续添加物之前，利用所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比与所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值的比较，以确定所述第二连续添加物的组成。在一些实例中，如果在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比等于或大于所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。在一些实例中，如果在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比等于或大于所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含所述 X-OH 或水。

[0213] 在一些实施方案中，所述接触可以包括，为所述第二反应混合物中氯代亚磷酸酯的转化率规定预定目标值。所述接触还可以包括，在添加第一连续添加物之后，确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率。如果在所述第一反应混合物中作为所述 CLS 和所述 TLS 存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，则所述第二连续添加物包含水。如果在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含水或具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。如果在所述第一反应混合物中作为所述 CLS 或作为所述 TLS 存

在的磷的摩尔百分比都不等于或不高于所述最终反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比的相应预定极限值，并且所述第一反应产物中氯代亚磷酸酯的所述转化率小于第二反应混合物中氯代亚磷酸酯的所述转化率的预定目标值，则所述第二连续添加物包含足够量的所述X-OH，使得所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率等于或高于所述第二反应混合物中所述氯代亚磷酸酯的所述转化率的预定目标值。在一些实例中，如果在所述第一反应混合物中作为所述CLS存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含具有化学结构$R^1$-OH或$R^2$-OH的醇。

[0214] 在一些实施方案中，接触包括，为所述第二反应混合物中氯代亚磷酸酯的转化率规定预定目标值。接触还可以包括，在添加第一连续添加物之后，确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率和确定所述第一反应混合物中作为LHP存在的磷的摩尔百分比。如果在所述第一反应混合物中作为所述CLS和所述TLS存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比的相应预定极限值，则所述第二连续添加物包含水。如果在所述第一反应混合物中作为所述CLS存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为LHP存在的磷的摩尔百分比等于或大于所述最终反应混合物中作为LHP存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含具有化学结构$R^1$-OH或$R^2$-OH的醇；并且如果在所述第一反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比都不等于或不高于所述最终反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比的相应预定极限值，并且所述第一反应产物中氯代亚磷酸酯的所述转化率小于第二反应混合物中氯代亚磷酸酯的所述转化率的预定目标值，则第二连续添加物包含足够量的X-OH，使得所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率等于或高于所述第二反应混合物中所述氯代亚磷酸酯的所述转化率的预定目标值。在一些实例中，如果在所述第一反应混合物中作为所述CLS存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为LHP存在的磷的摩尔百分比不等于或大于所述最终反应混合物中作为LHP存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含水或具有化学结构$R^1$-OH或$R^2$-OH的醇；并且如果在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述CLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为LHP存在的磷的摩尔百分比不等于或大于所述最终反应混合物中LHP含量的预定极限值，则所述第二添加物包含水。在一些实例中，如果在所述第一反应混合物中作为所述CLS存

在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为LHP存在的磷的摩尔百分比不等于或大于所述最终反应混合物中作为LHP存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含所述X-OH；并且，如果在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述CLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为LHP存在的磷的摩尔百分比不等于或大于所述最终反应混合物中LHP含量的预定极限值，则所述第二添加物不包含水或具有化学结构$R^1$-OH或$R^2$-OH的醇。

[0215] 在一些实施方案中，在第一连续添加中添加的所述X-OH与在第二连续添加中添加的所述X-OH的重量比为9.0：1.0至9.9：1.0。

[0216] 任选的第三连续添加

[0217] 所述接触还包括进行第三添加步骤，或者所述最终反应混合物是所述第二反应混合物。如果所述接触包括进行第三添加步骤，则所述最终反应混合物不是第二反应混合物。如果所述接触不包括进行第三添加步骤，则所述最终反应混合物是第二反应混合物。

[0218] 在进行的情况下的所述第三添加步骤包括，任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述X-OH、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物的量。在一些实施方案中，如果进行第三添加步骤，进行以下步骤：利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定在第三连续添加中添加的选自由所述X-OH、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物的量。在其他实施方案中，如果进行第三添加步骤，不进行以下步骤：利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定在第三连续添加中添加的选自由所述X-OH、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物的量。在进行的情况下的所述第三添加步骤包括，任选地确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比。在一些实施方案中，如果进行所述第三添加步骤，进行以下步骤：确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比。在其他实施方案中，如果进行所述第三添加步骤，不进行以下步骤：确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比。在进行的情况下的所述第三添加步骤包括，向所述第二反应混合物添加第三连续添加物，包括选自由所述X-OH、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，以提供最终反应混合物。

[0219] 在一些实施方案中，所述接触包括，利用所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值来确定在所述第三连续添加中添加的所述X-OH的量，以使作为所述至少一种副产物存在于所述最终反应混合物中的磷的摩尔百分比

小于所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值。

[0220] 在一些实例中，在所述第三连续添加（如果进行）中添加的所述X-OH的量等于或小于在所述第二连续添加中添加的所述X-OH的量。在一些实例中，在所述第三连续添加中添加的所述X-OH的量为零。在一些实例中，如果在所述第三连续添加中添加的所述X-OH的量为零，则在进行的情况下的所述第三连续添加物包含水或具有化学结构$R^1$-OH或$R^2$-OH的醇中的至少一种。

[0221] 在一些实施方案中，利用作为所述CLS存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值的比较确定在所述第三连续添加（如果进行）中添加的化合物的量，包括在所述第三添加中添加一定量的选自由所述X-OH、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，所述一定量足以使作为所述CLS存在于所述最终反应混合物中的磷的摩尔百分比等于或低于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值。在一些实例中，如果作为所述CLS存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三连续添加物包含水或具有化学结构$R^1$-OH或$R^2$-OH的醇。在一些实例中，如果作为所述CLS存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三添加物不包含所述X-OH。

[0222] 在一些实施方案中，利用作为所述TLS存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值的比较确定在所述第三连续添加中添加的化合物的量，包括在所述第三添加中添加一定量的选自由所述X-OH、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，所述一定量足以使作为所述TLS存在于所述最终反应混合物中的磷的摩尔百分比等于或低于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值。在一些实例中，如果作为所述TLS存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三连续添加物包含水。在一些实例中，如果作为TLS存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三连续添加物不包含所述X-OH或所述具有化学结构$R^1$-OH或$R^2$-OH的醇。

[0223] 在一些实施方案中，利用作为所述TLS存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值的比较，确定在所述第三连续添加中添加的化合物的量，包括在所述第三添加中添加一定量的选自由所述X-OH、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，所述一定量足以使作为所述TLS存在于所述最终反应混合物中的磷的摩尔百分比等于或低于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值。在一些实例中，如果作为所述TLS存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第

三连续添加物包含水。在一些实例中，如果作为TLS存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三连续添加物不包含所述X-OH或所述具有化学结构$R^1$-OH或$R^2$-OH的醇。

[0224] 在一些实例中，如果所述第二反应混合物中所述氯代亚磷酸酯的转化率小于约100％，则所述接触还包括将所述第三连续添加物添加至所述第二反应混合物，其中所述第三连续添加物包含足够量的水或具有化学结构$R^1$-OH或$R^2$-OH的醇，使得在所述第三连续添加之后，在所述最终反应混合物中的所述氯代亚磷酸酯转化率为约100％。

[0225] 在一些实例中，接触包括，确定所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率和确定所述第二反应混合物中作为TLS存在的磷的摩尔百分比，其中如果所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率小于约100％，并且如果在所述第二反应混合物中作为TLS存在的磷的摩尔百分比小于所述最终反应混合物中作为TLS存在的磷的摩尔百分比的预定极限值，则还包括将所述第三连续添加物添加至所述第二反应混合物，其中所述第三连续添加物包含足够量的具有化学结构$R^1$-OH或$R^2$-OH的醇，使得在所述第三连续添加之后，在所述最终反应混合物中的所述氯代亚磷酸酯的转化率为约100％。

[0226] 在一些实施方案中，如果所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率小于约100％，并且如果在所述第二反应混合物中作为LHP存在的磷的摩尔百分比小于所述最终反应混合物中作为LHP存在的磷的摩尔百分比的预定极限值，则所述接触还包括将第三连续添加物添加至所述第二反应混合物，其中所述第三连续添加物包含足够量的水，使得在所述第三连续添加之后，在所述最终反应混合物中的所述氯代亚磷酸酯的转化率为约100％。

[0227] 在一些实施方案中，第一连续添加物包含足够量的所述X-OH，使得所述第一反应混合物中所述氯代亚磷酸酯的转化率为约85％至约95％。在所述第二连续添加之后，所述第二反应混合物中所述氯代亚磷酸酯的所述转化率可以为约95％至约99％。所述第三连续添加物可以包含足够量的水和具有化学结构$R^1$-OH或$R^2$-OH的醇，使得所述最终反应混合物中所述氯代亚磷酸酯的转化率为约100％。

[0228] <u>预测</u>

[0229] 在多个实施方案中，利用所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的所述转化率的预定目标值的比较，来确定要在所述第二连续添加中添加的所述X-OH的量，包括预测工序。所述预测可以是任何适合的预测，其中在第二添加中添加的X-OH的量足以产生尽可能多的DLS并且消耗尽可能多的氯代亚磷酸酯，而不引起副产物的水平超过最终反应混合物中副产物水平的预定极限值。在所述第二添加之后，可以利用添加水或通过添加具有结构$R^1$-OH或$R^2$-OH的醇消耗所述第二反应混合物中所述氯代亚磷酸酯的剩余部分（如果存在的话，例如如果所述第二反应混合物不是所述最终反应混合物）。如果使用第三添加，可以使用任何适合的方法估算在所述第三添加中添加的、用于消耗所述氯代亚磷酸酯的剩余部分的水或醇的量，如使用在如以下所述的多个转化率范围的选择性比率。

[0230] 所述预测工序可以包括，利用在给定的转化率范围的所述氯代亚磷酸酯至所述含磷配体和CLS的至少一个选择性比率来预测氯代亚磷酸酯的最大百分比转化率，使得在所

述第二反应混合物中的所述预测的百分比转化率下，所述第二反应混合物中作为CLS存在的磷的百分比小于所述最终反应混合物中作为CLS存在的磷的百分比的预定极限值。所述预测工序还可以包括，将第二反应混合物中氯代亚磷酸酯的所述转化率的预定目标值设定为所述氯代亚磷酸酯的所述预测的最大百分比转化率。所述预测工序还可以包括，在所述第二连续添加中添加一定量的所述X-OH，所述一定量足以使所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率约等于所述第二反应混合物中所述氯代亚磷酸酯的所述转化率的预定目标值。

[0231] 在一些实施方案中，在给定的转化率范围的所述氯代亚磷酸酯至所述含磷配体和CLS的所述选择性比率包括对于至多约98％的转化率，例如对于约90％至约98％的转化率，例如约1∶6的CLS与含磷配体的摩尔选择性比率。在一些实例中，在给定的转化率范围的所述氯代亚磷酸酯至所述含磷配体和CLS的所述选择性比率包括对于约98％至约100％之间的转化率而言约1∶1的CLS与含磷配体的摩尔选择性比率。

[0232] 在实施方案中，在给定的转化率范围的所述氯代亚磷酸酯至所述含磷配体和CLS的所述选择性比率可以在任何适合的转化率范围存在。例如，氯代亚磷酸酯的转化率范围可以为约0％至约20％、约0％至约50％、约0％至约90％、约0％至约95％、约0％至约100％、约20％至约40％、约40％至约60％、约60％至约80％、或约80％至约100％。在实施方案中，在给定的转化率范围的选择性比率可以是任何适合的选择性比率，例如，在给定的转化率范围，氯代亚磷酸酯至含磷配体和CLS的选择性比率可以为约1∶(0.001-1000)，如约1∶0.001、1∶0.01、1∶0.1、1∶1、1∶2、1∶4、1∶6、1∶8、1∶10、1∶12、1∶14、1∶16、1∶18、1∶20、1∶100、或约1∶1000摩尔比。在一些实例中，选择性比率可以是实验确定的。

[0233] 在一些实施方案中，预测工序可以包括，利用在给定的转化率范围的所述氯代亚磷酸酯至所述含磷配体和TLS的至少一个选择性比率来预测氯代亚磷酸酯的最大百分比转化率，使得在所述第二反应混合物中在所述预测的百分比转化率下，所述第二反应混合物中作为TLS存在的磷的百分比小于所述最终反应混合物中作为TLS存在的磷的百分比的预定极限值。所述预测工序还可以包括，将第二反应混合物中氯代亚磷酸酯的所述转化率的预定目标值设定为所述氯代亚磷酸酯的所述预测的最大百分比转化率。所述预测工序还可以包括，在所述第二连续添加中添加一定量的所述X-OH，所述一定量足以使所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率约等于所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率的所述预定目标值。

[0234] 在一些实施方案中，在给定的转化率范围的所述氯代亚磷酸酯至所述含磷配体和TLS的所述选择性比率包括对于至多约98％的转化率而言，例如对于约90％至约98％的转化率而言，约1∶6的TLS与含磷配体的摩尔选择性比率。在一些实例中，在给定的转化率范围的所述氯代亚磷酸酯至所述含磷配体和TLS的所述选择性比率包括对于约98％与约100％之间的转化率而言约1∶1的TLS与含磷配体的摩尔选择性比率。

[0235] 在实施方案中，在给定的转化率范围的所述氯代亚磷酸酯至所述含磷配体和TLS的所述选择性比率可以在任何适合的转化率范围存在。例如，氯代亚磷酸酯的转化率范围可以为约0％至约20％、约0％至约50％、约0％至约90％、约0％至约95％、约0％至约100％、约20％至约40％、约40％至约60％、约60％至约80％、或约80％至约100％。在实施方案中，在给定的转化率范围的选择性比率可以是任何适合的选择性比率，例如，在给

定的转化率范围，氯代亚磷酸酯至含磷配体和TLS的选择性比率可以为约1：(0.001-100)，如约1：0.001、1：0.01、1：0.1、1：1、1：2、1：4、1：6、1：8、1：10、1：12、1：14、1：16、1：18、1：20、1：100、或约1：1000摩尔比。在一些实例中，选择性比率可以是实验确定的。

[0236] 可重复性

[0237] 在本发明的一些实施方案中，所述最终反应混合物的杂质水平或产率在精密公差(tight tolerance)内是高度可重复的。这可以是本发明超过制造含磷配体的其他方法的主要优点。

[0238] 例如，在一些实施方案中，在所述方法的多次重复之间的含磷配体的百分产率在5％之内。在多个实施方案中，在多次重复之间的含磷配体的百分产率可以始终在1％、2％、3％、4％、5％、6％、7％、8％、9％、10％、15％、20％、25％之内。对于一贯性而言，可以实现2、3、4、5、10、15、20、40、60、80、100、500、或超过1000次公差，而不发生故障。

[0239] 在一些实施方案中，最终产物混合物中作为TLS存在的磷的百分比在所述方法的多次重复之间的作为TLS存在的磷的百分比的5％之内。在多个实施方案中，在多次重复之间的最终产物混合物中作为TLS存在的磷的百分比可以始终在1％、2％、3％、4％、5％、6％、7％、8％、9％、10％、15％、20％、25％之内。对于一贯性而言，可以实现2、3、4、5、10、15、20、40、60、80、100、500、或超过1000次公差，而不发生故障。

[0240] 在一些实施方案中，最终产物混合物中作为CLS存在的磷的百分比在所述方法的多次重复之间的作为CLS存在的磷的百分比的5％之内。在多个实施方案中，在多次重复之间的最终产物混合物中作为TLS存在的磷的百分比可以始终在1％、2％、3％、4％、5％、6％、7％、8％、9％、10％、15％、20％、25％之内。对于一贯性而言，可以实现2、3、4、5、10、15、20、40、60、80、100、500、或超过1000次公差，而不发生故障。

[0241] 在一些实施方案中，最终产物混合物中作为LHP存在的磷的百分比在所述方法的多次重复之间的作为LHP存在的磷的百分比的5％之内。在多个实施方案中，在多次重复之间的最终产物混合物中作为TLS存在的磷的百分比可以始终在1％、2％、3％、4％、5％、6％、7％、8％、9％、10％、15％、20％、25％之内。对于一贯性而言，可以实现2、3、4、5、10、15、20、40、60、80、100、500、或超过1000次公差，而不发生故障。

[0242] 在一些实施方案中，可以实现多种副产物或产率的公差的任何一个或任何组合。

## 实施例

[0243] 通过参照以下通过说明的方式提供的实施例，可以更好的理解本发明。本发明并不限于在本文中给出的实施例。

[0244] 在以下实施例中使用的设备是：玻璃内衬反应器（标称容量约630L，内部直径约1,000mm，外套表面积约3.2$m^2$)、叶轮（约480mm直径，4个间隔叶桨，向下泵送，最大搅拌速度188rpm)、在反应器的相对的两侧的2个指形挡板(finger baffle)、位于叶轮顶端附近的2个单独的进料管（在指形挡板内部的4mm直径聚四氟乙烯(PTFE)管）、样品抽取系统、和热电偶（在指形挡板内）。没有金属组分与流体、玻璃内衬反应器、玻璃被覆的搅拌器和挡板、或PTFE进料管接触。

[0245] 在操作期间，使用手动控制的具有基于重量损失的调节（称量刻度）的正位移活塞泵将进料添加至反应器。在添加期间，搅拌反应混合物并且通过使用夹套冷却(jacket cooling）将反应温度控制为约 50℃。

[0246] 在以下实施例中，方法目标是使 DLS 产率最大化，同时将最终反应混合物中副产物的量限制为约 3 摩尔％的作为 CLS 存在的磷的最大值和限制为约 3 摩尔％的作为 LHP 存在的磷的最大值。

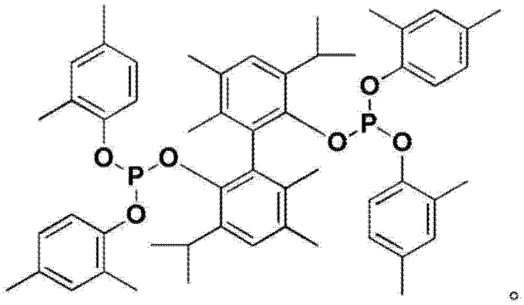
[0247] 在所有实施例中，使用与由 PCT 公开 WO2004/050588 描述的方法相似的方法生成氯代亚磷酸酯起始混合物。在约 50℃，在搅拌的情况下，向在甲苯（300kg）中的三氯化磷（25kg）的混合物添加 2,4- 二甲苯酚（45.5kg）和三乙胺（39kg）。

[0248] 在所有实施例中，使用以下步骤：使用磷核磁共振光谱法（$^{31}$P NMR）以确定起始混合物的磷分布并且使用此分析以计算三乙胺和联芳化合物的第一连续剂量，以将在第一反应混合物中约 90％氯代亚磷酸酯转化率作为目标。(b) 在第一连续剂量之后，使用 $^{31}$P NMR 以确定第一反应混合物的磷分布并且使用此分析以计算（例如预测）联芳化合物的第二连续剂量以将第二反应混合物中 CLS 含量限制为约 3 摩尔％的磷的最大值（例如，以添加尽可能多的联芳而不引起第二反应混合物中 CLS 含量超过最终反应混合物中 CLS 含量的预定极限值）。(c) 在得到第二反应混合物的第二连续添加之后，通过将第三添加物、小过量的 2,4- 二甲苯酚添加至第二反应混合物以得到最终反应混合物，从而完成氯代亚磷酸酯转化。在每个情况下，舍弃将水添加至第二反应混合物代替 2,4- 二甲苯酚以完成氯代亚磷酸酯转化的选择方案，因为这将会超过 LHP 浓度最大值（例如将会超过最终反应混合物中 LHP 含量的预定极限值）。(d) 在第三添加之后，使用 $^{31}$P NMR 以确定最终产物混合物的磷分布并且使用此分析以确认方法目标已经实现。

[0249] 在以下实施例中，具体选择性比率是针对各种的氯代亚磷酸酯转化率范围使用的。这些仅是针对各种的转化率范围的具体选择性比率的实例，也可以使用其他选择性比率。在一个实施例中，可以实验确定具体选择性比率。

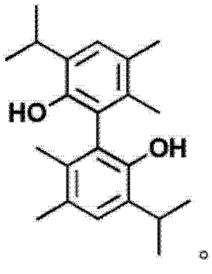
[0250] 在以下实施例中，所形成的 DLS 结构具有以下化学结构：

[0251]



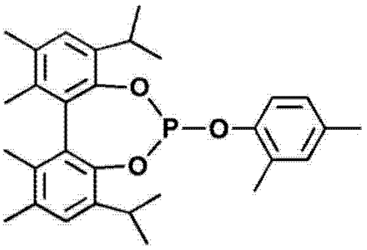
[0252] 在以下实施例中，所添加的联芳化合物具有以下结构：

[0253]



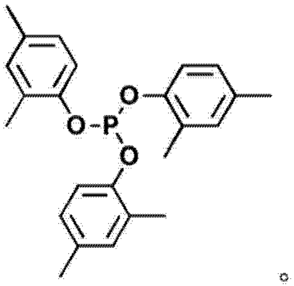
[0254] 在以下实施例中,所形成的 CLS 结构具有以下结构 :

[0255]



[0256] 在以下实施例中,所形成的 TLS 结构具有以下结构 :

[0257]



[0258] <u>实施例 1</u>

[0259] 磷分布 - 起始混合物

[0260]

| 含磷组分 | 摩尔% P(近似) | Kg(近似) |
|---|---|---|
| DLS | 0 | 0 |
| TLS | 8 | 5.7 |
| CLS | 0 | 0 |
| 氯代亚磷酸酯 | 87 | 48.7 |
| LHP | 2 | |
| 其他 | 3 | |

[0261] 第一连续剂量 - 按一个部分向搅拌的悬浮液添加化学计量过量的三乙胺(20.3kg),接着在约 2 小时内连续添加溶解于甲苯(36 重量%)中的联芳化合物(22.3kg)。然后通过 $^{31}$P NMR 分析反应混合物。

[0262] 磷分布 - 第一反应混合物

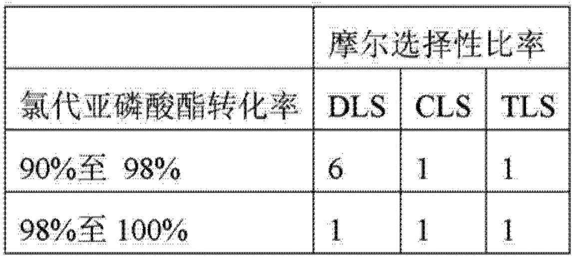
[0263]

| 含磷组分 | 摩尔% P(近似) | Kg(近似) |
|---|---|---|
| DLS | 69 | 54.7 |
| TLS | 14 | 10.1 |
| CLS | 2 | 1.7 |
| 氯代亚磷酸酯 | 10 | 5.6 |
| LHP | 3 | |
| 其他 | 2 | |

[0264]　第二连续剂量-通过运行副产物积累模型来计算第二连续剂量。使用针对相应的氯代亚磷酸酯转化率范围的选择性比率，预测到，如果联芳添加持续进行以完成氯代亚磷酸酯转化，最终反应混合物中作为CLS存在的磷的摩尔百分比将会超过3%。

[0265]　在各个转化率范围的选择性比率

[0266]



| | 摩尔选择性比率 | | |
|---|---|---|---|
| 氯代亚磷酸酯转化率 | DLS | CLS | TLS |
| 90%至 98% | 6 | 1 | 1 |
| 98%至 100% | 1 | 1 | 1 |

[0267]　副产物积累模型

[0268]

| 氯代亚磷酸酯百分比转化率 | CLS(摩尔) | TLS(摩尔) |
|---|---|---|
| 10 | 2.00 | 14.00 |
| 9 | 2.13 | 14.13 |
| 8 | 2.25 | 14.25 |
| 7 | 2.38 | 14.38 |
| 6 | 2.50 | 14.50 |
| 5 | 2.63 | 14.63 |
| 4 | 2.75 | 14.75 |
| 3 | 2.88 | 14.88 |

| | | |
|---|---|---|
| 2 | 3.00 | 15.00 |
| 1 | 3.33 | 15.33 |
| 0 | 3.67 | 15.67 |

[0269]

[0270] 在约 60 分钟内向搅拌的悬浮液添加额外量的联芳化合物 (2.7kg)，以第二反应混合物中氯代亚磷酸酯的约 2% 转化率为目标。接着添加足以完成氯代亚磷酸酯的转化的剂量的 2,4- 二甲苯酚 (0.5kg)，外加小过量。然后通过 $^{31}$P NMR 分析最终反应混合物。

[0271] 磷分布 - 最终反应混合物

[0272]

| 含磷组分 | 摩尔% P( 近似 ) | Kg( 近似 ) |
|---|---|---|
| DLS | 76 | 60.3 |
| TLS | 16 | 11.5 |
| CLS | 3 | 2.6 |
| 氯代亚磷酸酯 | 0 | 0 |
| LHP | 2 | |
| 其他 | 3 | |

[0273] <u>实施例 2</u>

[0274] 磷分布 - 起始混合物

[0275]

| 含磷组分 | 摩尔% P( 近似 ) | Kg( 近似 ) |
|---|---|---|
| DLS | 0 | 0 |
| TLS | 9 | 6.5 |
| CLS | 0 | 0 |
| 氯代亚磷酸酯 | 86 | 48.1 |
| LHP | 1 | |
| 其他 | 4 | |

[0276] 第一连续剂量 - 以一个部分向搅拌的悬浮液添加化学计量过量的三乙胺 (22kg)，并且在约 2 小时内连续添加溶解于甲苯 (30.5 重量% ) 中的联芳化合物 (22.8kg)。然后通

过 $^{31}$P NMR 分析反应混合物。

[0277]　磷分布－第一反应混合物

[0278]

| 含磷组分 | 摩尔％ P（近似） | Kg（近似） |
|---|---|---|
| DLS | 68 | 53.9 |
| TLS | 15 | 10.5 |
| CLS | 2.4 | 2.1 |
| 氯代亚磷酸酯 | 10.3 | 5.6 |
| LHP | 2.3 | |
| 其他 | 2 | |

[0279]　第二连续剂量－预测到，在约 95％氯代亚磷酸酯转化率下，第二反应混合物中作为 CLS 存在的磷的百分比将会达到 3％。

[0280]　在各个转化率范围的选择性比率

[0281]

| | 摩尔选择性比率 | | |
|---|---|---|---|
| 氯代亚磷酸酯转化率 | DLS | CLS | TLS |
| 90%至 98% | 6 | 1 | 1 |
| 98%至 100% | 1 | 1 | 1 |

[0282]　副产物积累模型

[0283]

| 氯代亚磷酸酯转化率 | CLS（摩尔） | TLS（摩尔） |
|---|---|---|
| 10 | 2.40 | 14.60 |
| 9 | 2.53 | 14.73 |
| 8 | 2.65 | 14.85 |
| 7 | 2.78 | 14.98 |
| 6 | 2.90 | 15.10 |
| 5 | 3.03 | 15.23 |
| 4 | 3.15 | 15.35 |

| | | |
|---|---|---|
| 3 | 3.28 | 15.48 |
| 2 | 3.40 | 15.60 |
| 1 | 3.73 | 15.93 |
| 0 | 4.07 | 16.27 |

[0284]

[0285] 在约 60 分钟内向搅拌的悬浮液添加额外量的联芳化合物 (2.5kg)，以约 5%氯代亚磷酸酯转化率为目标，接着添加小剂量的 2,4- 二甲苯酚 (0.9kg)。然后通过 $^{31}P$ NMR 分析最终反应混合物。

[0286] 磷分布 - 最终产物混合物

[0287]

| 含磷组分 | 摩尔% P(近似) | Kg(近似) |
|---|---|---|
| DLS | 75 | 57.1 |
| TLS | 19 | 14.4 |
| CLS | 3 | 2.6 |
| 氯代亚磷酸酯 | 0 | 0 |
| LHP | 2 | |
| 其他 | 1 | |

[0288] 实施例 3

[0289] 磷分布 - 起始混合物

[0290]

| 含磷组分 | 摩尔% P(近似) | Kg(近似) |
|---|---|---|
| DLS | 0 | 0 |
| TLS | 11.4 | 8.3 |
| CLS | 0 | 0 |
| 氯代亚磷酸酯 | 81 | 45.6 |
| LHP | 3.6 | |
| 其他 | 4 | |

[0291] 第一连续剂量 - 以一个部分向搅拌的悬浮液添加化学计量过量的三乙胺 (21kg)，

并且在约 2 小时内连续添加溶解于甲苯（35.4 重量％）中的联芳化合物（22.3kg）。然后通过 $^{31}P$ NMR 分析第一反应混合物。

[0292] 磷分布－第一反应混合物

[0293]

| 含磷组分 | 摩尔％ P（近似） | Kg（近似） |
|---|---|---|
| DLS | 66.6 | 52.8 |
| TLS | 13.3 | 9.5 |
| CLS | 2 | 1.7 |
| 氯代亚磷酸酯 | 11.8 | 6.6 |
| LHP | 2.6 | |
| 其他 | 3.7 | |

[0294] 第二连续剂量－预测到，在约 96％氯代亚磷酸酯转化率下，第二反应混合物中作为 CLS 存在的磷的摩尔百分比将会达到约 3％。

[0295] 在各个转化率范围的选择性比率

[0296]

| | 摩尔选择性比率 | | |
|---|---|---|---|
| 氯代亚磷酸酯转化率 | DLS | CLS | TLS |
| 90%至 98% | 6 | 1 | 1 |
| 98%至 100% | 1 | 1 | 1 |

[0297] 副产物积累模型

[0298]

| 氯代亚磷酸酯转化率 | CLS（摩尔） | TLS（摩尔） |
|---|---|---|
| 11.8 | 2.00 | 13.30 |
| 10 | 2.23 | 13.53 |
| 9 | 2.35 | 13.65 |
| 8 | 2.48 | 13.78 |
| 7 | 2.60 | 13.90 |
| 6 | 2.73 | 14.03 |
| 5 | 2.85 | 14.15 |

| | | |
|---|---|---|
| 4 | 2.98 | 14.28 |
| 3 | 3.10 | 14.40 |
| 2 | 3.43 | 14.73 |
| 1 | 3.77 | 15.07 |
| 0 | 4.10 | 15.40 |

[0299] 在约 60 分钟内向搅拌的悬浮液添加额外量的联芳化合物（2.7kg），以第二反应混合物中约 4%氯代亚磷酸酯转化率为目标，接着添加小剂量的 2,4- 二甲苯酚（1.0kg）。然后通过 $^{31}$P NMR 分析最终反应混合物。

[0300] 磷分布 - 最终产物混合物

[0301]

| 含磷组分 | 摩尔% P（近似） | Kg（近似） |
|---|---|---|
| DLS | 71.5 | 56.3 |
| TLS | 20.5 | 14.1 |
| CLS | 3.4 | 2.9 |
| 氯代亚磷酸酯 | 0 | 0 |
| LHP | 2.6 | |
| 其他 | 2 | |

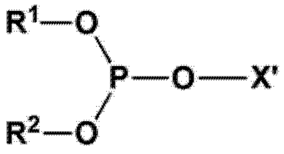
[0302] 已经采用的术语和表述用作描述的术语而且是非限制性的，并且并非意在通过使用此类术语和表述排除示出的和描述的特征或其一部分的任何等价物，而是了解到在要求保护的本发明的范围内可以存在多种修改。因此，应理解的是，尽管通过优选的实施方案和任选的特征已经具体地公开了本发明，可以由本领域技术人员采取在本文中公开的概念的修改和变化，并且此类修改和变化被认为在如由所附权利要求定义的本发明的范围之内。

[0303] 额外的实施方案。

[0304] 本发明提供以下示例性实施方案，其编号不应被解释为表示重要程度：

[0305] 实施方案 1 提供一种用于制备具有以下化学结构的含磷配体结构的方法，

[0306]

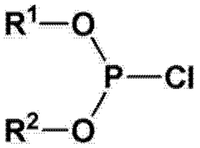


结构 I'

[0307] 所述方法包括：

[0308] 使以下结构的氯代亚磷酸酯，

[0309]



结构 II

[0310] 与具有化学结构 X-OH 的化合物和有机叔胺接触，以提供包含所述配体结构的最终反应混合物；

[0311] 其中所述接触包括：

[0312] 为所述最终反应混合物中作为至少一种副产物存在的磷的摩尔百分比规定预定极限值；

[0313] 在第一连续添加中将所述 X-OH 添加至所述氯代亚磷酸酯中，以提供第一反应混合物；

[0314] 确定作为所述至少一种副产物存在于所述第一反应混合物中的磷的摩尔百分比；

[0315] 利用作为所述至少一种副产物存在于所述第一反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第二连续添加中添加的选自由所述 X-OH、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量；

[0316] 向所述第一反应混合物添加第二连续添加物，包括选自由所述 X-OH、水、或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供第二反应混合物；以及

[0317] 或者

[0318] 进行第三添加步骤，所述第三添加步骤包括

[0319] 任选地确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比；

[0320] 任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述 X-OH、水、和所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量；以及

[0321] 向所述第二反应混合物添加第三连续添加物，包括选自由所述 X-OH、水、和所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供所述最终反应混合物；

[0322] 或者

[0323] 所述最终反应混合物是所述第二反应混合物；

[0324] 其中在结构 I’和 II 中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^1$ 和 $R^2$ 彼此桥接或彼此不桥接；并且 X 和 X’中的每一个独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、亚磷酸酯基联芳基、亚磷酸酯基联杂芳基、羟基联芳基、羟基联杂芳基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团。

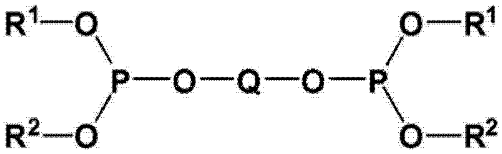
[0325]　实施方案 2 提供实施方案 1 所述的方法，其中进行第三添加步骤并且所述第三添加步骤还包括：

[0326]　确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比；以及

[0327]　利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述 X-OH、水、和所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量。

[0328]　实施方案 3 提供实施方案 1-2 中任一项所述的方法，其中所述结构 I’的配体结构是具有结构 I 的化学结构的二亚磷酸酯配体结构 (DLS)，

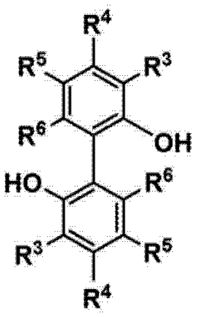
[0329]



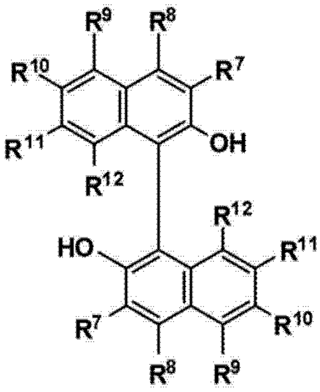
结构 I

[0330]　其中所述 X-OH 是选自由结构 III、结构 IV 和结构 V 组成的组的联芳化合物，

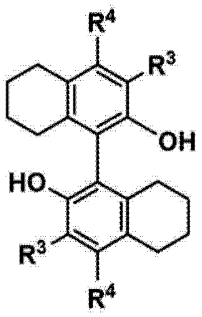
[0331]



结构 III



结构 IV

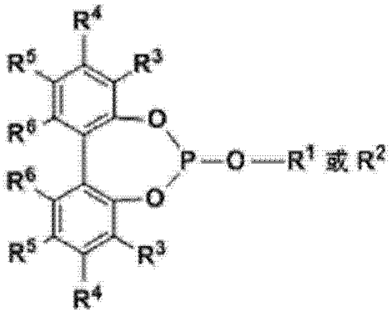


结构 V;

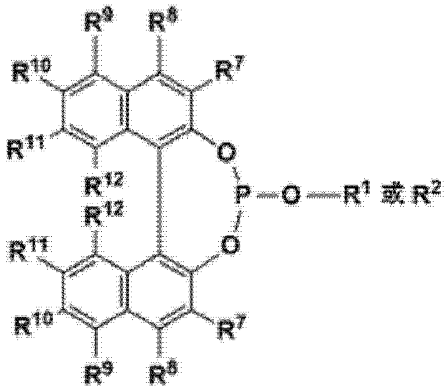
[0332]　其中在结构 I-V 中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和 $R^{12}$ 中的每一个独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团；并且 O-Q-O 是所述联芳化合物的二价物种。

[0333]　实施方案 4 提供实施方案 1-3 中任一项所述的方法，其中所述至少一种副产物包含 C-phite 配体结构 (CLS)，该 C-phite 配体结构具有如下显示为结构 VI、VII、或 VIII 的化学结构：

[0334]

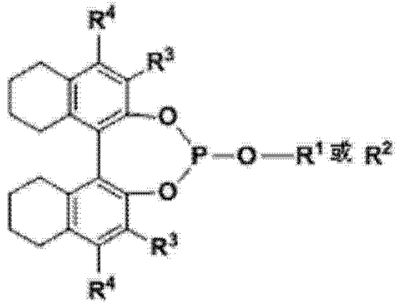


结构 VI



结构 VII

[0335]



结构 VIII

[0336]　其中在结构 VI-VIII 中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^1$ 和 $R^2$ 彼此桥接或彼此不桥接；并且 $R^3$、$R^4$、$R^5$、$R^6$、$R^7$、$R^8$、$R^9$、$R^{10}$、$R^{11}$、和 $R^{12}$ 中的每一个独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团；

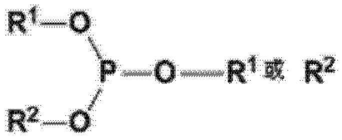
[0337]　其中为所述最终反应混合物中作为至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为 CLS 存在的磷的摩尔百分比规定预定极限值。

[0338]　实施方案 5 提供实施方案 4 所述的方法，其中在所述最终反应混合物中，作为所述含磷配体结构存在的磷的百分比大于或等于约 65％，并且作为所述 CLS 存在的磷的百分比小于约 5％。

[0339]　实施方案 6 提供实施方案 4-5 中任一项所述的方法，其中在所述最终反应混合物中，作为所述含磷配体结构存在的磷的百分比大于或等于约 70％，并且作为所述 CLS 存在的磷的百分比小于约 3.5％。

[0340]　实施方案 7 提供实施方案 1-6 中任一项所述的方法，其中所述至少一种副产物包含 T-phite 配体结构（TLS），该 T-phite 配体结构具有如下显示为结构 IX 的化学结构：

[0341]



[0342]

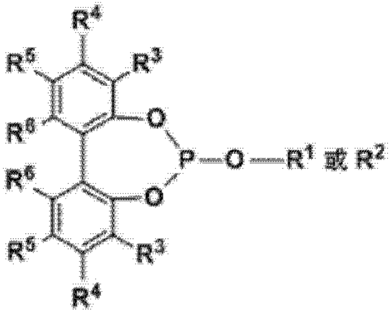
**结构 IX；**

[0343] 其中在结构 IX 中，$R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；并且 $R^1$ 和 $R^2$ 彼此桥接或彼此不桥接；

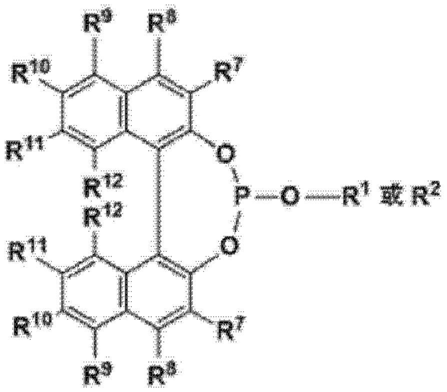
[0344] 其中为所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为 TLS 存在的磷的摩尔百分比规定预定极限值。

[0345] 实施方案 8 提供实施方案 1-7 中任一项所述的方法，其中所述至少一种副产物包含 C-phite 配体结构 (CLS)，该 C-phite 配体结构具有如下显示为结构 VI、VII、或 VIII 的化学结构：

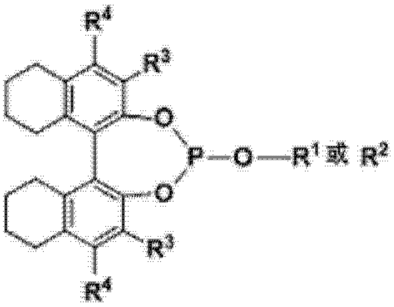
[0346]



**结构 VI**



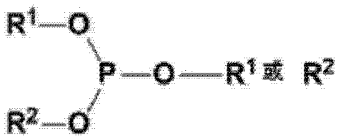
**结构 VII**



**结构 VIII**

[0347] 其中所述至少一种副产物还包含 T-phite 配体结构 (TLS)，该 T-phite 配体结构具有如下显示为结构 IX 的化学结构：

[0348]



**结构 IX；**

[0349] 其中在结构 VI-VIII 和 IX 中，R$^{1}$ 和 R$^{2}$ 是相同或不同的、取代或未取代的单价芳基；R$^{1}$ 和 R$^{2}$ 彼此桥接或彼此不桥接；并且 R$^{3}$、R$^{4}$、R$^{5}$、R$^{6}$、R$^{7}$、R$^{8}$、R$^{9}$、R$^{10}$、R$^{11}$、和 R$^{12}$ 中的每一个独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团；

[0350] 其中为所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为 TLS 存在的磷的摩尔百分比规定预定极限值；

[0351] 其中为所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为 CLS 存在的磷的摩尔百分比规定预定极限值。

[0352] 实施方案 9 提供实施方案 1-8 中任一项所述的方法，其中所述至少一种副产物包含配体水解产物 (LHP)，所述配体水解产物包含通过包括以下各项的过程得到的产物：

[0353] 所述含磷配体或所述氯代亚磷酸酯的水解；

[0354] 衍生自所述含磷配体或衍生自所述氯代亚磷酸酯的产物的水解；或

[0355] 所述含磷配体的水解产物或所述氯代亚磷酸酯的水解产物的反应，或衍生自所述含磷配体或衍生自所述氯代亚磷酸酯的产物的水解产物的反应；

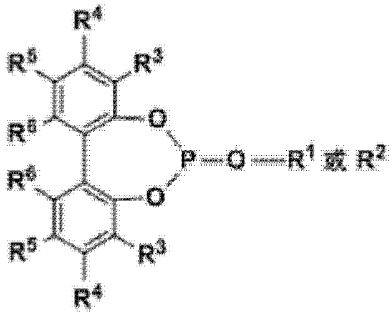
[0356] 其中为所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比规定预定极限值。

[0357] 实施方案 10 提供实施方案 9 所述的方法，其中在所述最终反应混合物中，作为所述含磷配体结构存在的磷的百分比大于或等于约 65%，并且作为所述 LHP 存在的磷的百分比小于不大于约 5%。

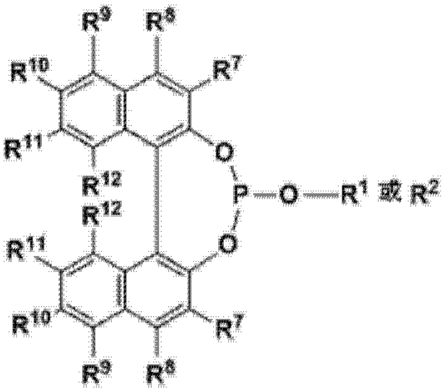
[0358] 实施方案 11 提供实施方案 9-10 中任一项所述的方法，其中在所述最终反应混合物中，作为所述含磷配体结构存在的磷的百分比大于或等于约 70%，并且作为所述 LHP 存在的磷的百分比小于不大于约 3.5%。

[0359] 实施方案 12 提供实施方案 1-11 中任一项所述的方法，其中所述至少一种副产物包含 C-phite 配体结构 (CLS)，该 C-phite 配体结构具有如下显示为结构 VI、VII、或 VIII 的化学结构：

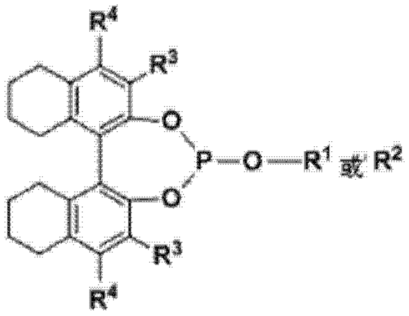
[0360]



**结构 VI**



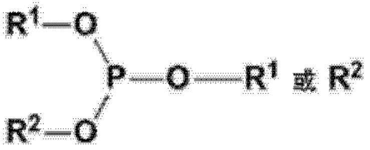
**结构 VII**



**结构 VIII;**

[0361] 其中所述至少一种副产物还包含 T-phite 配体结构（TLS），该 T-phite 配体结构具有如下显示为结构 IX 的化学结构：

[0362]



**结构 IX;**

[0363] 其中在结构 VI-VIII 和 IX 中，R$^{1}$ 和 R$^{2}$ 是相同或不同的、取代或未取代的单价芳基；R$^{1}$ 和 R$^{2}$ 彼此桥接或彼此不桥接；并且 R$^{3}$、R$^{4}$、R$^{5}$、R$^{6}$、R$^{7}$、R$^{8}$、R$^{9}$、R$^{10}$、R$^{11}$、和 R$^{12}$ 中的每一个独立地选自由以下各项组成的组：氢、烷基、芳基、杂芳基、芳氧基、杂芳氧基、烷氧基、烷氧基烷基、缩醛基、芳氧羰基、烷氧羰基、芳基羰基、烷基羰基、噁唑基、胺基、酰胺基、腈基、巯基、和卤素基团；

[0364] 其中为所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为 TLS 存在的磷的摩尔百分比规定预定极限值；

[0365] 其中为所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为 CLS 存在的磷的摩尔百分比规定预定

极限值；

[0366] 其中所述至少一种副产物还包含配体水解产物(LHP)，所述配体水解产物包含通过包括以下各项的过程得到的产物：

[0367] 所述含磷配体或所述氯代亚磷酸酯的水解；

[0368] 衍生自所述含磷配体或衍生自所述氯代亚磷酸酯的产物的水解；或

[0369] 所述含磷配体的水解产物或所述氯代亚磷酸酯的水解产物的反应，或衍生自所述含磷配体或衍生自所述氯代亚磷酸酯的产物的水解产物的反应；

[0370] 其中为所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比规定预定极限值包括为所述最终反应混合物中作为LHP存在的磷的摩尔百分比规定预定极限值。

[0371] 实施方案13提供实施方案1-12中任一项所述的方法，其中所述接触还包括利用所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值来确定要在所述第一或第二连续添加中添加的所述X-OH的量，以使作为所述至少一种副产物存在于所述第一或第二反应混合物中的磷的摩尔百分比小于所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值。

[0372] 实施方案14提供实施方案2-13中任一项所述的方法，其中所述接触还包括利用所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值来确定要在所述第三连续添加中添加的所述X-OH的量，以使作为所述至少一种副产物存在于所述最终反应混合物中的磷的摩尔百分比小于所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值。

[0373] 实施方案15提供实施方案1-14中任一项所述的方法，其中在所述第二连续添加中添加的所述X-OH的量小于在所述第一连续添加中添加的所述X-OH的量；并且其中在进行的情况下的所述第三连续添加中添加的所述X-OH的量等于或小于在所述第二连续添加中添加的所述X-OH的量。

[0374] 实施方案16提供实施方案1所述的方法，其中在所述第二或第三连续添加中添加的所述X-OH的量为零。

[0375] 实施方案17提供实施方案1-16中任一项所述的方法，其中如果在所述第二连续添加中添加的所述X-OH的量为零，则所述第二连续添加物包含水或所述具有化学结构$R^1$-OH或$R^2$-OH的醇中的至少一种；并且其中如果在所述第三连续添加中添加的所述X-OH的量为零，则在进行的情况下的所述第三连续添加物包含水或所述具有化学结构$R^1$-OH或$R^2$-OH的醇中的至少一种。

[0376] 实施方案18提供实施方案4-17中任一项所述的方法，其中利用作为所述CLS存在于所述第一或第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值的比较以确定要在所述第二连续添加中或要在进行的情况下的所述第三连续添加中添加的化合物的量包括：在所述第二或第三添加中添加一定量的选自由所述X-OH、水、和所述具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，所述一定量足以使所述第二或最终反应混合物中作为所述CLS存在的磷的摩尔百分比等于或低于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值。

[0377] 实施方案19提供实施方案18所述的方法，其中如果作为所述CLS存在于所述

第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含水或所述具有化学结构$R^1$-OH或$R^2$-OH的醇；并且其中如果作为所述CLS存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三连续添加物包含水或所述具有化学结构$R^1$-OH或$R^2$-OH的醇。

[0378] 实施方案20提供实施方案18-19中任一项所述的方法，其中如果作为所述CLS存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含所述X-OH；并且其中如果作为所述CLS存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三添加物不包含所述X-OH。

[0379] 实施方案21提供实施方案7-20中任一项所述的方法，其中利用作为所述TLS存在于所述第一或第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值的比较来确定要在所述第二或第三连续添加中添加的化合物的量包括：在所述第二或第三添加中添加一定量的选自由所述X-OH、水、和所述具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，所述一定量足以使所述第二或最终反应混合物中作为所述TLS存在的磷的摩尔百分比等于或低于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值。

[0380] 实施方案22提供实施方案21所述的方法，其中如果作为所述TLS存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含水；并且其中如果作为所述TLS存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三连续添加物包含水。

[0381] 实施方案23提供实施方案21-22所述的方法，其中如果作为TLS存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含所述X-OH或所述具有化学结构$R^1$-OH或$R^2$-OH的醇；并且其中如果作为TLS存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三连续添加物不包含所述X-OH或所述具有化学结构$R^1$-OH或$R^2$-OH的醇。

[0382] 实施方案24提供实施方案9-23中任一项所述的方法，其中利用作为所述LHP存在于所述第一或第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述LHP存在的磷的摩尔百分比的预定极限值的比较来确定要在所述第二或第三连续添加中添加的化合物的量包括：在所述第二或第三添加中添加一定量的选自由所述X-OH、水、和所述具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，所述一定量足以使作为所述LHP存在于所述第二或最终反应混合物中的磷的摩尔百分比等于或低于所述最终反应混合物中作为所述LHP存在的磷的摩尔百分比的预定极限值。

[0383] 实施方案 25 提供实施方案 24 所述的方法，其中如果作为 LHP 存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 LHP 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含所述 X-OH 或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇；并且其中如果作为 LHP 存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 LHP 存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三连续添加物包含所述 X-OH 或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。

[0384] 实施方案 26 提供实施方案 24-25 中任一项所述的方法，其中如果作为 LHP 存在于所述第一反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 LHP 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含水；并且其中如果作为 LHP 存在于所述第二反应混合物中的磷的摩尔百分比等于或大于所述最终反应混合物中作为所述 LHP 存在的磷的摩尔百分比的预定极限值，则在进行的情况下的所述第三连续添加物不包含水。

[0385] 实施方案 27 提供实施方案 8-26 中任一项所述的方法，其中如果在所述第一反应混合物中作为所述 CLS 和所述 TLS 存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，则所述第二连续添加物包含水；并且其中如果在所述第二反应混合物中作为所述 CLS 和所述 TLS 存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，则在进行的情况下的所述第三连续添加物包含水。

[0386] 实施方案 28 提供实施方案 8-27 中任一项所述的方法，其中如果在所述第一反应混合物中作为所述 CLS 和所述 TLS 存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，则所述第二连续添加物不包含所述 X-OH 或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇；并且其中如果在所述第二反应混合物中作为所述 CLS 和所述 TLS 存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，则在进行的情况下的所述第三连续添加物不包含所述 X-OH 或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。

[0387] 实施方案 29 提供实施方案 1-28 所述的方法，其中所述接触还包括：

[0388] 为所述第二反应混合物中氯代亚磷酸酯的转化率规定预定目标值；

[0389] 在添加第一连续添加物之后，确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率；以及

[0390] 在添加所述第二连续添加物之前，利用所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值的比较，以确定要在所述第二连续添加中添加的所述 X-OH 的量。

[0391] 实施方案 30 提供实施方案 8-29 中任一项所述的方法，其中所述接触还包括：

[0392] 为所述第二反应混合物中氯代亚磷酸酯的转化率规定预定目标值；

[0393] 在添加第一连续添加物之后，确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率；以及

[0394] 在添加所述第二连续添加物之前，利用所述第一反应混合物中所述氯代亚磷酸酯

的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值的比较，以确定要在所述第二连续添加中添加的所述 X-OH 的量。

[0395] 实施方案 31 提供实施方案 30 所述的方法，其中如果在所述第一反应混合物中作为所述 CLS 或作为所述 TLS 存在的磷的摩尔百分比都不等于或不高于所述最终反应混合物中作为所述 CLS 或作为所述 TLS 存在的磷的摩尔百分比的相应预定极限值，并且所述第一反应混合物中氯代亚磷酸酯的转化率小于所述最终反应混合物中氯代亚磷酸酯的转化率的预定目标值，则要在所述第二连续添加中添加的所述 X-OH 的量足以使所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率等于或高于所述第二反应混合物中所述氯代亚磷酸酯的转化率的预定目标值。

[0396] 实施方案 32 提供实施方案 30-31 中任一项所述的方法，其中如果在所述第一反应混合物中作为所述 CLS 或作为所述 TLS 存在的磷的摩尔百分比都不等于或不高于所述最终反应混合物中作为所述 CLS 或作为所述 TLS 存在的磷的摩尔百分比的相应预定极限值，并且所述第一反应混合物中氯代亚磷酸酯的转化率小于所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值，则所述第二连续添加物不包含水或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。

[0397] 实施方案 33 提供实施方案 1 或 29 所述的方法，其中如果所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率小于约 100％，则所述方法还包括将所述第三连续添加物添加至所述第二反应混合物，其中所述第三连续添加物包含足够量的水或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇，使得在第三连续添加之后，在所述最终反应混合物中的氯代亚磷酸酯转化率为约 100％。

[0398] 实施方案 34 提供实施方案 7-33 中任一项所述的方法，所述方法还包括确定所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率，并且确定所述第二反应混合物中作为 TLS 存在的磷的摩尔百分比，其中如果所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率小于约 100％，并且如果在所述第二反应混合物中作为 TLS 存在的磷的摩尔百分比小于所述最终反应混合物中作为 TLS 存在的磷的摩尔百分比的预定极限值，则所述方法还包括将所述第三连续添加物添加至所述第二反应混合物，其中所述第三连续添加物包含足够量的所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇，使得在第三连续添加之后，在所述最终反应混合物中的所述氯代亚磷酸酯的转化率为约 100％。

[0399] 实施方案 35 提供实施方案 9-34 中任一项所述的方法，其中如果所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率小于约 100％，并且如果在所述第二反应混合物中作为 LHP 存在的磷的摩尔百分比小于所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值，则所述方法还包括将第三连续添加物添加至所述第二反应混合物，其中所述第三连续添加物包含足够量的水，使得在第三连续添加之后，在所述最终反应混合物中的所述氯代亚磷酸酯的转化率为约 100％。

[0400] 实施方案 36 提供实施方案 35 所述的方法，其中在所述第三连续添加之后，在所述最终反应混合物中作为所述含磷配体结构存在的磷的百分比大于或等于约 65％并且作为所述 LHP 存在的磷的百分比小于约 5％。

[0401] 实施方案 37 提供实施方案 35-36 中任一项所述的方法，其中在所述第三连续添加之后，在所述最终反应混合物中作为所述含磷配体结构存在的磷的百分比大于或等于约

70％，并且作为所述 LHP 存在的磷的百分比小于约 3.5％。

[0402] 实施方案 38 提供实施方案 1-37 中任一项所述的方法，其中所述接触还包括 ：

[0403] 为所述第一反应混合物中氯代亚磷酸酯的转化率规定预定目标值 ；

[0404] 在添加第一连续添加物之前，利用所述第一反应混合物中氯代亚磷酸酯的转化率的预定目标值，以确定要在所述第一连续添加中添加的所述 X-OH 的量，使得所述第一反应混合物中氯代亚磷酸酯的转化率等于或高于所述第一反应混合物中氯代亚磷酸酯的转化率的预定目标值。

[0405] 实施方案 39 提供实施方案 9-38 中任一项所述的方法，其中所述接触还包括 ：

[0406] 为所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比规定预定极限值 ；

[0407] 在添加第一连续添加物之后，确定所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比 ；以及

[0408] 在添加所述第二连续添加物之前，利用所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比与所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值的比较，以确定所述第二连续添加物的组成。

[0409] 实施方案 40 提供实施方案 12-39 中任一项所述的方法，其中所述接触还包括 ：

[0410] 为所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比规定预定极限值 ；

[0411] 在添加第一连续添加物之后，确定所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比 ；以及

[0412] 在添加所述第二连续添加物之前，利用所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比与所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值的比较，以确定所述第二连续添加物的组成。

[0413] 实施方案 41 提供实施方案 40 所述的方法，其中如果在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比等于或大于所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。

[0414] 实施方案 42 提供实施方案 40-41 中任一项所述的方法，其中如果在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比等于或大于所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含所述 X-OH 或水。

[0415] 实施方案 43 提供实施方案 8-42 中任一项所述的方法，其中所述接触还包括 ：

[0416] 为所述第二反应混合物中氯代亚磷酸酯的转化率规定预定目标值 ；以及

[0417] 在添加第一连续添加物之后，

[0418] 确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率 ；以及

[0419] 其中如果在所述第一反应混合物中作为所述 CLS 和所述 TLS 存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，则所述第二连续添加物包含水；

[0420] 其中如果在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含水或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇；并且

[0421] 其中如果在所述第一反应混合物中作为所述 CLS 或作为所述 TLS 存在的磷的摩尔百分比都不等于或不高于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，并且所述第一反应产物中氯代亚磷酸酯的转化率小于第二反应混合物中氯代亚磷酸酯的转化率的预定目标值，则所述第二连续包含足够量的所述 X-OH，使得所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率等于或高于所述第二反应混合物中所述氯代亚磷酸酯的转化率的预定目标值。

[0422] 实施方案 44 提供实施方案 43 所述的方法，其中如果在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇。

[0423] 实施方案 45 提供实施方案 12-44 中任一项所述的方法，其中所述接触还包括：

[0424] 为所述第二反应混合物中氯代亚磷酸酯的转化率规定预定目标值；以及

[0425] 在添加第一连续添加物之后，

[0426] 确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率；以及

[0427] 确定所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比；

[0428] 其中如果在所述第一反应混合物中作为所述 CLS 和所述 TLS 存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，则所述第二连续添加物包含水；

[0429] 其中如果在所述第一反应混合物中作为所述 CLS 存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述 CLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述 TLS 存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为 LHP 存在的磷的摩尔百分比等于或大于所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇；并且

[0430] 其中如果在所述第一反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比都不等于或不高于所述最终反应混合物中作为所述 CLS 或所述 TLS 存在的磷的摩尔百分比的相应预定极限值，并且所述第一反应产物中氯代亚磷酸酯的转化率小于所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值，则第二连续添加物包含足够量的 X-OH，使得所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率等于或高于所述第二反应混

合物中所述氯代亚磷酸酯的转化率的预定目标值。

[0431] 实施方案46提供实施方案45所述的方法，其中接触还包括：

[0432] 其中如果在所述第一反应混合物中作为所述CLS存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为LHP存在的磷的摩尔百分比不等于或大于所述最终反应混合物中作为LHP存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物包含水或所述具有化学结构$R^1$-OH或$R^2$-OH的醇；并且

[0433] 其中如果在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述CLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为LHP存在的磷的摩尔百分比不等于或大于所述最终反应混合物中LHP含量的预定极限值，则所述第二添加物包含水。

[0434] 实施方案47提供实施方案45-46中任一项所述的方法，其中接触还包括：

[0435] 其中如果在所述第一反应混合物中作为所述CLS存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为LHP存在的磷的摩尔百分比不等于或大于所述最终反应混合物中作为LHP存在的磷的摩尔百分比的预定极限值，则所述第二连续添加物不包含所述X-OH；并且

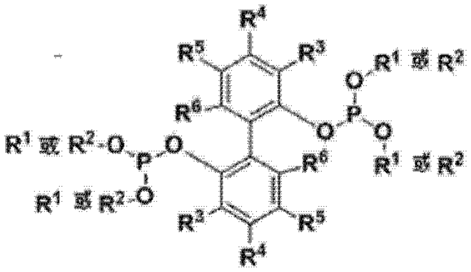
[0436] 其中如果在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为所述CLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值，并且在所述第一反应混合物中作为LHP存在的磷的摩尔百分比不等于或大于所述最终反应混合物中LHP含量的预定极限值，则所述第二添加物不包含水或所述具有化学结构$R^1$-OH或$R^2$-OH的醇。

[0437] 实施方案48提供实施方案1-47中任一项所述的方法，其中所述第一反应混合物具有化学计量过量的氯代亚磷酸酯。

[0438] 实施方案49提供实施方案1-48中任一项所述的方法，其中所述接触在化学计量过量的有机叔胺的存在下进行。

[0439] 实施方案50提供实施方案1-49中任一项所述的方法，其中所述含磷配体具有以下化学结构：

[0440]



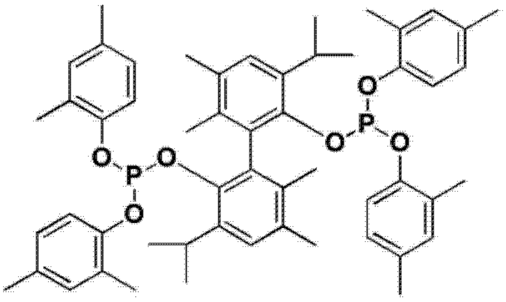
[0441] 其中 $R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

[0442] 实施方案 51 提供实施方案 1-50 中任一项所述的方法，其中 $R^2 = R^1$，其中 $R^1$ 是单价二甲苯基。

[0443] 实施方案 52 提供实施方案 1-51 中任一项所述的方法，其中 $R^2 = R^1$，其中 $R^1$ 是单价 2,4- 二甲苯基。

[0444] 实施方案 53 提供实施方案 1-52 中任一项所述的方法，其中所述含磷配体具有以下化学结构：

[0445]



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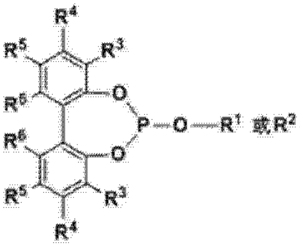
[0446] 实施方案 54 提供实施方案 4-53 中任一项所述的方法，其中所述 CLS 具有以下化学结构：

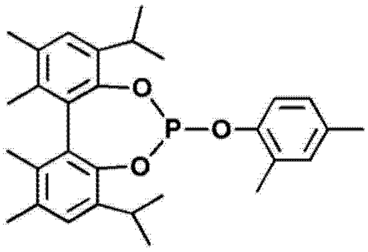
[0447]



[0448] 其中 $R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；$R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

[0449] 实施方案 55 提供实施方案 4-54 中任一项所述的方法，其中所述 CLS 具有以下化学结构：

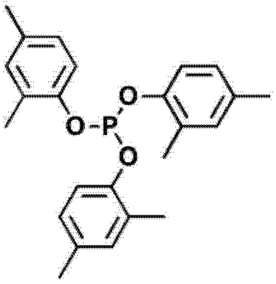
[0450]



[0451] 实施方案56提供实施方案7-55中任一项所述的方法，其中所述TLS具有化学结构$P(OR^1)_3$，其中$R^1$是取代或未取代的芳基。

[0452] 实施方案57提供实施方案7-56中任一项所述的方法，其中所述TLS具有以下化学结构：

[0453]



[0454] 实施方案58提供实施方案1-57中任一项的方法，其中所述有机叔胺包括三烷基胺。

[0455] 实施方案59提供实施方案1-58中任一项的方法，其中所述有机叔胺包括三乙胺。

[0456] 实施方案60提供实施方案4-59中任一项所述的方法，其中所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值小于或等于约5%。

[0457] 实施方案61提供实施方案4-60中任一项所述的方法，其中所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值小于或等于约3%。

[0458] 实施方案62提供实施方案30、43、或45中任一项所述的方法，其中利用所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值的比较以确定要在所述第二连续添加中添加的所述X-OH的量包括：

[0459] 利用在给定的转化率范围下的所述氯代亚磷酸酯至所述含磷配体和CLS的至少一个选择性比率来预测氯代亚磷酸酯的最大百分比转化率，使得在所述第二反应混合物中的所述预测的百分比转化率下，所述第二反应混合物中作为CLS存在的磷的百分比小于所述最终反应混合物中作为CLS存在的磷的百分比的预定极限值；

[0460] 将所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值设定为所述氯代亚磷酸酯的所述预测的最大百分比转化率；以及

[0461] 在所述第二连续添加中添加一定量的所述X-OH，所述一定量足以使所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率约等于所述第二反应混合物中所述氯代亚磷酸酯的转化率的预定目标值。

[0462] 实施方案63提供实施方案62所述的方法，其中在给定的转化率范围下的所述氯代亚磷酸酯至所述含磷配体和CLS的选择性比率包括对于至多约98%的转化率而言约1：

6 的 CLS 与含磷配体的摩尔选择性比率。

[0463] 实施方案 64 提供实施方案 62-63 中任一项所述的方法，其中在给定的转化率范围下的所述氯代亚磷酸酯至所述含磷配体和 CLS 的选择性比率包括对于约 98%至约 100%之间的转化率而言约 1 :1 的 CLS 与含磷配体的摩尔选择性比率。

[0464] 实施方案 65 提供实施方案 7-64 中任一项所述的方法，其中所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值小于或等于约 30%。

[0465] 实施方案 66 提供实施方案 7-65 中任一项所述的方法，其中所述最终反应混合物中作为所述 TLS 存在的磷的摩尔百分比的预定极限值小于或等于约 22%。

[0466] 实施方案 67 提供实施方案 30、43、或 45 中任一项所述的方法，其中利用所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值的比较以确定要在所述第二连续添加中添加的所述 X-OH 的量包括 :

[0467] 利用在给定的转化率范围下的所述氯代亚磷酸酯至所述含磷配体和 TLS 的至少一个选择性比率来预测氯代亚磷酸酯的最大百分比转化率，使得在所述第二反应混合物中的所述预测的百分比转化率下，所述第二反应混合物中作为 TLS 存在的磷的百分比小于所述最终反应混合物中作为 TLS 存在的磷的百分比的预定极限值 ;

[0468] 将所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值设定为所述氯代亚磷酸酯的所述预测的最大百分比转化率 ;以及

[0469] 在所述第二连续添加中添加一定量的所述 X-OH，所述一定量足以使所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率约等于所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率的预定目标值。

[0470] 实施方案 68 提供实施方案 67 所述的方法，其中在给定的转化率范围下的所述氯代亚磷酸酯至所述含磷配体和 CLS 的选择性比率包括对于至多约 98%的转化率而言约 1 :6 的 CLS 与含磷配体的摩尔选择性比率。

[0471] 实施方案 69 提供实施方案 67-68 中任一项所述的方法，其中在给定的转化率范围下的所述氯代亚磷酸酯至所述含磷配体和 CLS 的选择性比率包括对于约 98%至约 100%之间的转化率而言约 1 :1 的 CLS 与含磷配体的摩尔选择性比率。

[0472] 实施方案 70 提供实施方案 29、30、43、或 45 中任一项所述的方法，其中所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值为约 95%至约 100%。

[0473] 实施方案 71 提供实施方案 29、30、43、或 45 中任一项所述的方法，其中所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值为约 96%至约 99%。

[0474] 实施方案 72 提供实施方案 38-71 中任一项所述的方法，其中所述第一反应混合物中所述氯代亚磷酸酯的转化率的预定目标值为约 85%至约 95%。

[0475] 实施方案 73 提供实施方案 38-72 中任一项所述的方法，其中所述第一反应混合物中所述氯代亚磷酸酯的转化率的预定目标值为约 90%。

[0476] 实施方案 74 提供实施方案 39、40、或 45 中任一项所述的方法，其中所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值为约 5%。

[0477] 实施方案 75 提供实施方案 39、40、或 45 中任一项所述的方法，其中所述最终反应混合物中作为 LHP 存在的磷的摩尔百分比的预定极限值为约 3%。

[0478] 实施方案 76 提供实施方案 1-75 中任一项所述的方法，其中所述接触通过选自由以下步骤组成的组的至少一个步骤进行 ：

[0479] (i) 将所述 X-OH 进料至所述氯代亚磷酸酯和所述有机叔胺的混合物中 ；

[0480] (ii) 将所述 X-OH 和所述有机叔胺分别进料至所述氯代亚磷酸酯中 ；或

[0481] (iii) 将所述 X-OH 和所述有机叔胺以混合物形式进料至所述氯代亚磷酸酯中。

[0482] 实施方案 77. 提供实施方案 1-76 中任一项所述的方法，其中所述反应混合物还包含至少一种芳族烃溶剂。

[0483] 实施方案 78 提供实施方案 77 所述的方法，其中所述芳族溶剂包括甲苯。

[0484] 实施方案 79 提供实施方案 77-78 中任一项所述的方法，所述方法还包括将所述 X-OH 以包含所述 X-OH 和所述烃溶剂的溶液形式进料至所述氯代亚磷酸酯中。

[0485] 实施方案 80 提供通过实施方案 1-79 中任一项所述的方法制备的结构 I 的含磷配体。

[0486] 实施方案 81 提供实施方案 1-80 中任一项所述的方法，其中

[0487] 第一连续添加物包含足够量的所述 X-OH，使得所述第一反应混合物中所述氯代亚磷酸酯的转化率为约 85％至约 95％ ；并且

[0488] 所述第二连续添加物包含比在所述第一连续添加中添加的所述 X-OH 的量更小的量的所述 X-OH。

[0489] 实施方案 82 提供实施方案 1-81 中任一项所述的方法，其中

[0490] 第一连续添加物包含足够量的 X-OH，使得所述第一反应混合物中所述氯代亚磷酸酯的转化率为约 85％至约 90％ ；并且

[0491] 所述第二连续添加物包含足够量的所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇，使得在所述第二反应混合物中的氯代亚磷酸酯转化率为约 100％。

[0492] 实施方案 83 提供实施方案 1-82 中任一项所述的方法，其中

[0493] 第一连续添加物包含足够量的所述 X-OH，使得所述第一反应混合物中所述氯代亚磷酸酯的转化率为约 85％至约 95％ ；并且

[0494] 在所述第二连续添加之后，所述第二反应混合物中所述氯代亚磷酸酯的转化率为约 95％至约 99％ ；

[0495] 所述第三连续添加物包含足够量的水或所述具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇，使得所述最终反应混合物中所述氯代亚磷酸酯的转化率为约 100％。

[0496] 实施方案 84 提供实施方案 1-83 中任一项所述的方法，其中所述方法提供作为第一最终反应混合物的最终反应混合物，其中重复所述方法以提供第二最终反应混合物，其中所述第一最终反应混合物中所述含磷配体的产率在所述第二最终反应混合物中所述含磷配体的产率的 5％之内。

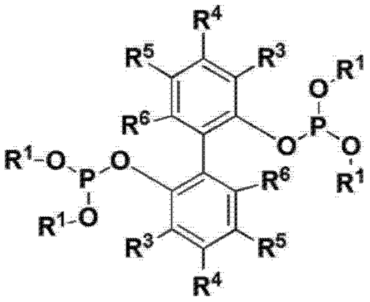
[0497] 实施方案 85 提供实施方案 4-84 中任一项所述的方法，其中所述方法提供作为第一最终反应混合物的最终反应混合物，其中重复所述方法以提供第二最终反应混合物，其中所述第一最终反应混合物中作为所述含磷配体、TLS、和 CLS 存在的磷的百分比各自分别在所述第二最终反应混合物中作为所述含磷配体、TLS、和 CLS 存在的磷的百分比的 5％之内。

[0498] 实施方案 86 提供实施方案 4-85 中任一项所述的方法，其中所述方法提供作为第

一最终反应混合物的最终反应混合物，其中重复所述方法以提供第二最终反应混合物，其中所述第一最终反应混合物中作为 CLS 存在的磷的百分比在所述第二最终反应混合物中作为所述 CLS 存在的磷的百分比的 5%之内。

[0499] 实施方案 87 提供一种用于制备具有以下结构的二亚磷酸酯配体结构（DLS）的方法，

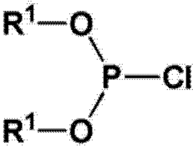
[0500]



[0501] 所述方法包括：

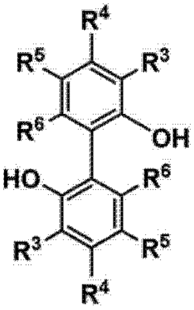
[0502] 使具有以下结构的氯代亚磷酸酯，

[0503]



[0504] 与具有以下结构的联芳化合物

[0505]

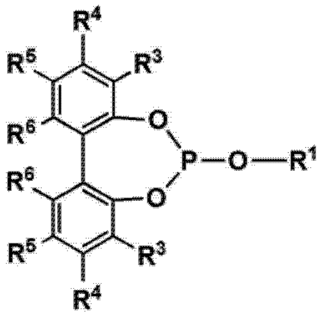


[0506] 和有机叔胺接触以提供包含所述二亚磷酸酯的最终反应混合物；

[0507] 其中所述接触包括

[0508] 为所述最终反应混合物中作为 C-phite 配体结构（CLS）存在的磷的摩尔百分比规定预定极限值，所述 C-phite 配体结构具有以下所示的化学结构：

[0509]



[0510] 在第一连续添加中将所述联芳化合物添加至所述氯代亚磷酸酯，使得在所述第一添加中添加的氯代亚磷酸酯的摩尔数大于在所述第一添加中添加的所述联芳化合物的摩尔数，以提供第一反应混合物；

[0511] 确定作为CLS存在于所述第一反应混合物中的磷的摩尔百分比；

[0512] 利用作为CLS存在于所述第一反应混合物中的磷的摩尔百分比与作为CLS存在的磷的摩尔百分比的预定极限值的比较，以确定要在第二连续添加中添加的选自由所述联芳化合物、水、和具有化学结构$R^1$-OH的醇中的至少一种组成的组的化合物的量，使得第二反应混合物中作为CLS存在的磷的摩尔百分比小于或等于所述最终反应混合物中作为CLS存在的磷的摩尔百分比的预定极限值；

[0513] 向所述第一反应混合物添加第二连续添加物，包括选自由所述联芳化合物、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，以提供所述第二反应混合物；以及

[0514] 或者

[0515] 进行第三添加步骤，所述第三添加步骤包括

[0516] 任选地确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比；

[0517] 任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述X-OH、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物的量；以及

[0518] 向所述第二反应混合物添加第三连续添加物，包括选自由所述X-OH、水、和所述具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，以提供最终反应混合物；

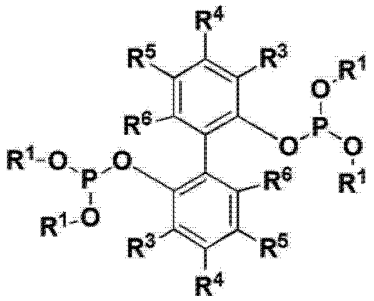
[0519] 或者

[0520] 所述最终反应混合物是所述第二反应混合物；

[0521] 其中$R^1$和$R^2$是相同或不同的、取代或未取代的单价芳基；$R^3$、$R^4$、$R^5$、$R^6$中的每一个独立地选自由氢和$C_{1-10}$烷基组成的组。

[0522] 实施方案88提供一种用于制备具有以下结构的二亚磷酸酯配体结构(DLS)的方法，

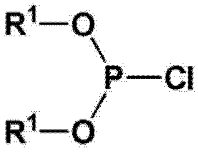
[0523]



[0524] 所述方法包括：

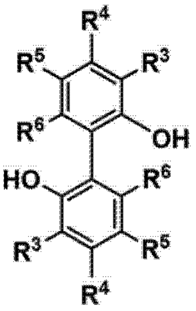
[0525] 使具有以下结构的氯代亚磷酸酯，

[0526]



[0527] 与具有以下结构的联芳化合物

[0528]

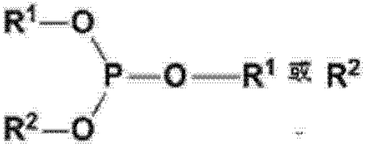


[0529] 和有机叔胺接触以提供包含所述二亚磷酸酯的最终反应混合物；

[0530] 其中所述接触包括

[0531] 为所述最终反应混合物中作为T-phite配体结构(TLS)存在的磷的摩尔百分比规定预定极限值，所述T-phite配体结构具有以下所示的化学结构

[0532]



；

[0533] 在第一连续添加中将所述联芳化合物添加至所述氯代亚磷酸酯，使得在所述第一添加中添加的氯代亚磷酸酯的摩尔数大于在所述第一添加中添加的联芳的摩尔数，以提供第一反应混合物；

[0534] 确定作为TLS存在于所述第一反应混合物中的磷的摩尔百分比；

[0535] 利用作为TLS存在于所述第一反应混合物中的磷的摩尔百分比与作为TLS存在的磷的摩尔百分比的预定极限值的比较，以确定要在第二连续添加中添加的选自由所述联芳化合物、水、和具有化学结构$R^1$-OH的醇组成的组的化合物的量，使得第二反应混合物中作

为TLS存在的磷的摩尔百分比小于或等于所述最终反应混合物中作为TLS存在的磷的摩尔百分比的预定极限值；

[0536] 向所述第一反应混合物添加第二连续添加物，包括选自由所述联芳化合物、水、和具有化学结构 $R^1$-OH或 $R^2$-OH的醇组成的组的化合物，以提供所述第二反应混合物；以及

[0537] 或者

[0538] 进行第三添加步骤，所述第三添加步骤包括

[0539] 任选地确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比；

[0540] 任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述X-OH、水、和所述具有化学结构 $R^1$-OH或 $R^2$-OH的醇组成的组的化合物的量；以及

[0541] 向所述第二反应混合物添加第三连续添加物，包括选自由所述X-OH、水、和具有化学结构 $R^1$-OH或 $R^2$-OH的醇组成的组的化合物，以提供最终反应混合物；

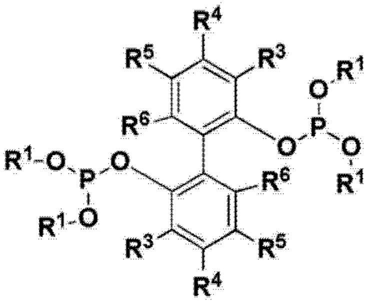
[0542] 或者

[0543] 所述最终反应混合物是所述第二反应混合物；

[0544] 其中 $R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；并且 $R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

[0545] 实施方案89提供一种用于制备具有以下结构的二亚磷酸酯配体结构(DLS)的方法，

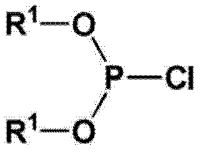
[0546]



[0547] 所述方法包括：

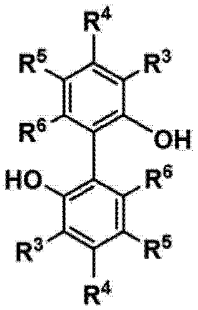
[0548] 使具有以下结构的氯代亚磷酸酯，

[0549]



[0550] 与具有以下结构的联芳化合物

[0551]



[0552] 和有机叔胺接触以提供包含所述二亚磷酸酯的最终反应混合物；

[0553] 其中所述接触包括

[0554] 为所述最终反应混合物中作为配体水解产物(LHP)存在的磷的摩尔百分比规定预定极限值，所述配体水解产物包含通过包括以下各项的过程得到的产物：

[0555] 所述DLS或所述氯代亚磷酸酯的水解；

[0556] 衍生自所述DLS或衍生自所述氯代亚磷酸酯的产物的水解；或

[0557] 所述DLS的水解产物或所述氯代亚磷酸酯的水解产物的反应，或衍生自所述DLS或衍生自所述氯代亚磷酸酯的产物的水解产物的反应；

[0558] 在第一连续添加中将所述联芳化合物添加至所述氯代亚磷酸酯，使得在所述第一添加中添加的氯代亚磷酸酯的摩尔数大于在所述第一添加中添加的联芳的摩尔数，以提供第一反应混合物；

[0559] 确定作为LHP存在于所述第一反应混合物中的磷的摩尔百分比；

[0560] 利用作为LHP存在于所述第一反应混合物中的磷的摩尔百分比与作为LHP存在的磷的摩尔百分比的预定极限值的比较，以确定要在第二连续添加中添加的选自由所述联芳化合物、水、和具有化学结构$R^1$-OH的醇组成的组的化合物的量，使得第二反应混合物中作为LHP存在的磷的摩尔百分比小于或等于所述最终反应混合物中作为LHP存在的磷的摩尔百分比的预定极限值；

[0561] 向所述第一反应混合物添加第二连续添加物，包括选自由所述联芳化合物、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，以提供所述第二反应混合物；以及

[0562] 或者

[0563] 进行第三添加步骤，所述第三添加步骤包括

[0564] 任选地确定作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比；

[0565] 任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由所述X-OH、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物的量；以及

[0566] 向所述第二反应混合物添加第三连续添加物，包括选自由所述X-OH、水、和具有化学结构$R^1$-OH或$R^2$-OH的醇组成的组的化合物，以提供最终反应混合物；

[0567] 或者

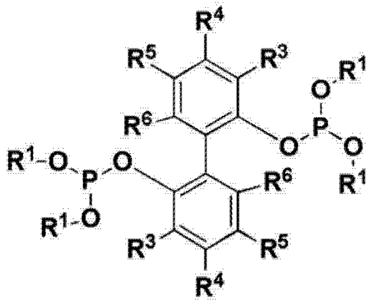
[0568] 所述最终反应混合物是所述第二反应混合物；

[0569] 其中$R^1$和$R^2$是相同或不同的、取代或未取代的单价芳基；并且$R^3$、$R^4$、$R^5$、$R^6$中的每

一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

[0570] 实施方案 90 提供一种用于制备具有以下结构的二亚磷酸酯配体结构（DLS）的方法，

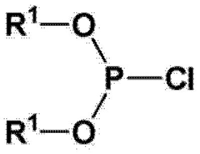
[0571]



[0572] 所述方法包括：

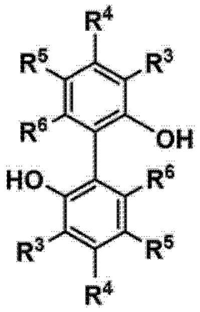
[0573] 使具有以下结构的氯代亚磷酸酯，

[0574]



[0575] 与具有以下结构的联芳化合物

[0576]

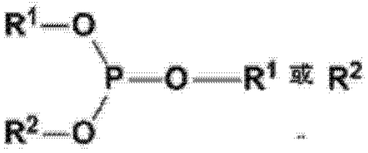


[0577] 和有机叔胺接触以提供包含所述二亚磷酸酯的最终反应混合物；

[0578] 其中所述接触包括

[0579] 为所述最终反应混合物中作为 T-phite 配体结构（TLS）存在的磷的摩尔百分比规定预定极限值，所述 T-phite 配体结构具有以下所示的化学结构

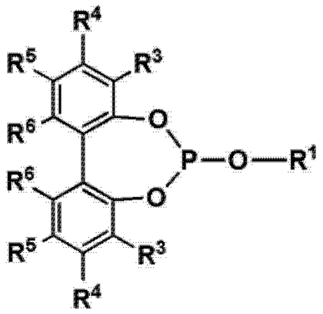
[0580]



；

[0581] 为所述最终反应混合物中作为 C-phite 配体结构（CLS）存在的磷的摩尔百分比规定预定极限值，所述 C-phite 配体结构具有以下所示的化学结构：

[0582]



[0583] 为所述最终反应混合物中作为配体水解产物(LHP)存在的磷的摩尔百分比规定预定极限值,所述配体水解产物包含通过包括以下各项的过程得到的产物：

[0584] 所述DLS或所述氯代亚磷酸酯的水解；

[0585] 衍生自所述DLS或衍生自所述氯代亚磷酸酯的产物的水解；或

[0586] 所述DLS的水解产物或所述氯代亚磷酸酯的水解产物的反应,或衍生自所述DLS或衍生自所述氯代亚磷酸酯的产物的水解产物的反应；

[0587] 为所述第一反应混合物中氯代亚磷酸酯的转化率规定预定目标值；

[0588] 在第一连续添加中将所述联芳化合物添加至所述氯代亚磷酸酯,以提供第一反应混合物,其中添加的联芳化合物的量足以使所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率等于或大于所述第一反应混合物中所述氯代亚磷酸酯的转化率的预定目标值；

[0589] 确定作为TLS存在于所述第一反应混合物中的磷的摩尔百分比；

[0590] 确定作为CLS存在于所述第一反应混合物中的磷的摩尔百分比；

[0591] 确定所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率；

[0592] 其中如果在所述第一反应混合物中作为所述CLS和所述TLS存在的磷的摩尔百分比都等于或大于所述最终反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比的相应预定极限值,则所述第二连续添加物包含水；

[0593] 其中如果在所述第一反应混合物中作为所述CLS存在的磷的摩尔百分比等于或高于所述最终反应混合物中作为所述CLS存在的磷的摩尔百分比的预定极限值,并且在所述第一反应混合物中作为所述TLS存在的磷的摩尔百分比不等于或不高于所述最终反应混合物中作为所述TLS存在的磷的摩尔百分比的预定极限值,并且在所述第一反应混合物中作为LHP存在的磷的摩尔百分比等于或大于所述最终反应混合物中作为LHP存在的磷的摩尔百分比的预定极限值,则所述第二连续添加物包含具有化学结构$R^1$-OH或$R^2$-OH的醇；

[0594] 其中如果在所述第一反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比都不等于或不高于所述最终反应混合物中作为所述CLS或所述TLS存在的磷的摩尔百分比的相应预定极限值,并且第一反应产物中氯代亚磷酸酯的转化率小于第二反应混合物中氯代亚磷酸酯的转化率的预定目标值,则第二连续添加物包含所述联芳化合物,其中要在所述第二连续添加中添加的所述联芳化合物的量通过以下方式确定：利用所述第一反应混合物中所述氯代亚磷酸酯的百分比转化率与所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值的比较,以确定要在所述第二连续添加中添加的所述联芳化合物的量,包括：

[0595] 将在给定的转化率范围下的所述氯代亚磷酸酯至所述含磷配体和CLS的至少一

个选择性比率与所述第一反应混合物中 TLS 和 CLS 的确定的摩尔百分比组合利用，以预测氯代亚磷酸酯的最大百分比转化率，使得在所述第二反应混合物中的所述预测的百分比转化率下，所述第二反应混合物中作为 CLS 存在的磷的百分比小于所述最终反应混合物中作为 CLS 存在的磷的百分比的预定极限值；以及

[0596] 将所述第二反应混合物中氯代亚磷酸酯的转化率的预定目标值设定为所述氯代亚磷酸酯的所述预测的最大百分比转化率；

[0597] 向所述第一反应混合物添加所述第二连续添加物，包括选自由所述联芳化合物、水、和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物，以提供所述第二反应混合物，其中如果在所述第二连续添加中添加联芳化合物，则所述第二连续添加中所述联芳化合物的量足以使所述第二反应混合物中所述氯代亚磷酸酯的百分比转化率约等于所述第二反应混合物中所述氯代亚磷酸酯的转化率的预定目标值；以及

[0598] 或者

[0599] 进行第三添加步骤，所述第三添加步骤包括

[0600] 任选地确定作为至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比；

[0601] 任选地利用作为所述至少一种副产物存在于所述第二反应混合物中的磷的摩尔百分比与所述最终反应混合物中作为所述至少一种副产物存在的磷的摩尔百分比的预定极限值的比较，以确定要在第三连续添加中添加的选自由水和具有化学结构 $R^1$-OH 或 $R^2$-OH 的醇组成的组的化合物的量；以及

[0602] 将第三连续添加物添加至所述第二反应混合物以提供所述最终反应混合物，其中在所述第三添加中添加的一种或多种化合物的量使得所述最终反应混合物中所述氯代亚磷酸酯的转化率为约 100%；

[0603] 或者

[0604] 所述最终反应混合物是所述第二反应混合物，其中在所述第二添加中添加的一种或多种化合物的量使得所述最终反应混合物中所述氯代亚磷酸酯的转化率为约 100%；

[0605] 其中 $R^1$ 和 $R^2$ 是相同或不同的、取代或未取代的单价芳基；并且 $R^3$、$R^4$、$R^5$、$R^6$ 中的每一个独立地选自由氢和 $C_{1-10}$ 烷基组成的组。

[0606] 实施方案 91 提供任选地配置使得可以使用或选择所叙述的全部要素或选项的实施方案 1-90 中任一项或任何组合的装置或方法。

[0607] 示例性的实施方案

[0608] 接触期间的摩尔比

[0609] 在一些实施方案中，可以控制某些摩尔比以提供对 DLS 形成的最佳选择性，和 CLS 和 TLS 形成的同时最佳的最小化，以及氯代亚磷酸酯的最佳转化率。存在多个可以控制的摩尔比，以及多种控制摩尔比的方法，其可以使得反应步骤优化。在本章节中描述的摩尔比仅是优化的实例，在一些实例中，控制这些摩尔比可以单独使用以优化所述方法；在本章节外还给出了可以在多个实施方案中单独使用或与本章节中给出的方法一起使用的其他优化方法（例如，其可以包括至少一些摩尔比的分析）。

[0610] 摩尔比 A 被定义为反应混合物中氯代亚磷酸酯的摩尔数与进料至反应混合物的联芳化合物的摩尔数的比值；例如，反应混合物中氯代亚磷酸酯的摩尔数除以进料至反应

混合物的联芳化合物的摩尔数。在一些实施方案中，可以通过控制所述接触的阶段期间的进料使得摩尔比 A 为至少约 2 而获得对形成 DLS 的高选择性。当摩尔比 A 为低于约 2 时，CLS 和 TLS 的形成增加，这降低了对 DLS 的选择性。在一些实施方案中，在具有高氯代亚磷酸酯转化率（例如在约 90％至约 100％之间）的所述接触的阶段期间，还可以通过控制进料使得摩尔比 A 在约 2.1 至约 2.7 之间而实现对希望的二亚磷酸酯的较高选择性。氯代亚磷酸酯转化率是添加至已经转化为其他材料的反应混合物的氯代亚磷酸酯的总摩尔数的百分比。

[0611] 摩尔比 B 被定义为来自进料至反应混合物的有机叔胺的碱性氮原子的摩尔数与反应混合物中氯代亚磷酸酯的摩尔数的比值；例如，来自进料至反应混合物的有机叔胺的碱性氮原子的摩尔数除以反应混合物中氯代亚磷酸酯的摩尔数。在一些实施方案中，可以通过控制所述接触的阶段期间的进料使得摩尔比 B 为至少约 1 而获得对 DLS 的形成的高选择性。在一些实施方案中，当摩尔比 B 为低于约 1 时，CLS 和 TLS 的形成可能会增加，这降低了对 DLS 形成的选择性。在一些实施方案中，可以通过控制进料使得摩尔比 B 在约 1.0 至约 1.5 之间，实现对希望的二亚磷酸酯的较高选择性。

[0612] 通过计算或另外确定存在于反应混合物中的氯代亚磷酸酯的总摩尔数、以及计算或另外确定来自进料至反应混合物的有机叔胺的碱性氮原子的摩尔数或者进料至反应混合物的联芳化合物的摩尔数中的至少一种，可以控制摩尔比 A 或 B。一旦确定摩尔比 A 或 B，则可以相应地调节氯代亚磷酸酯、有机叔胺、或联芳化合物中的至少一种的进料速率或添加量。在一些实施方案中，在没有显著的水（例如，以 $H_2O$ 重量计，＜约 300ppm）进入具有联芳化合物、有机叔胺、芳族烃溶剂，烃溶剂、或这些成员的组合的反应混合物的情况下，可以更容易地计算或另外确定这些量。在一些实施方案中，确定摩尔比 A 和 B 可以包括，抽取样品以分析液体反应混合物，例如通过 $^{31}P$ NMR、液相或气相色谱法、质谱法、或它们的任何组合。