PROCESS FOR PREPARING ANTIVIRAL COMPOUNDS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 61/444,475 filed February 18, 2011 and U.S. Provisional Application No. 61/365,293 filed July 16, 2010~~, the entire contents of which are incorporated herein by reference~~.

TECHNICAL FIELD

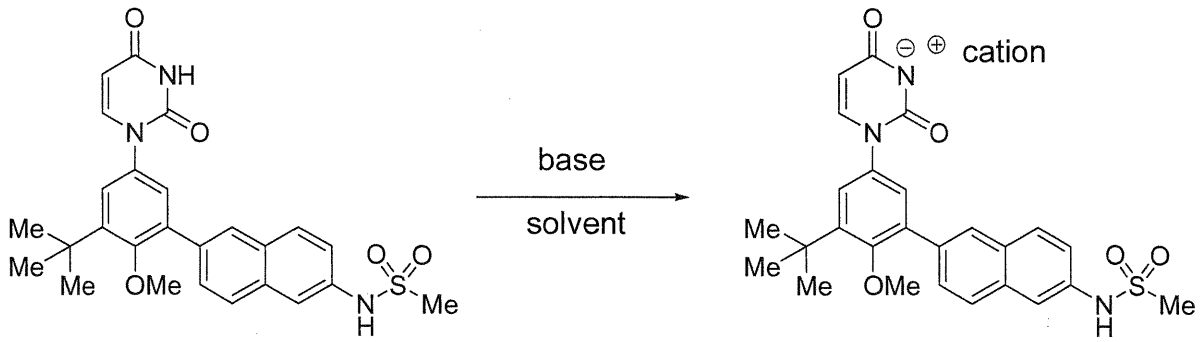
[0002] This disclosure is directed to: (a) processes for preparing a compound and salts thereof that, *inter alia*, are useful for inhibiting hepatitis C virus (HCV); (b) intermediates useful for the preparation of the compound and salts; (c) pharmaceutical compositions comprising the compound or salts; and (d) methods of use of such compositions.

BACKGROUND

[0003] Hepatitis C is a blood-borne, infectious, viral disease that is caused by a hepatotropic virus called HCV. At least six different HCV genotypes (with several subtypes within each genotype) are known to date. In North America, HCV genotype 1a predominates, followed by HCV genotypes 1b, 2a, 2b, and 3a. In the United States, HCV genotypes 1, 2, and 3 are the most common, with about 80% of the hepatitis C patients having HCV genotype 1. In Europe, HCV genotype 1b is predominant, followed by HCV genotypes 2a, 2b, 2c, and 3a. HCV genotypes 4 and 5 are found almost exclusively in Africa. As discussed below, the patient's HCV genotype is clinically important in determining the patient's potential response to therapy and the required duration of such therapy.

[0004] An HCV infection can cause liver inflammation (hepatitis) that is often asymptomatic, but ensuing chronic hepatitis can result in cirrhosis of the liver (fibrotic scarring of the liver), liver cancer, and/or liver failure. The World Health Organization estimates that about 170 million persons worldwide are chronically infected with HCV, and from about three to about four million persons are newly infected globally each year. According to the Centers for Disease Control and Prevention, about four million people in the United States are infected with HCV. Co-infection with the human immunodeficiency virus (HIV) is common, and rates of HCV infection among HIV positive populations are higher.

[0005] There is a small chance of clearing the virus spontaneously, but the majority of patients with chronic hepatitis C will not clear it without treatment. Indications for treatment typically include proven HCV infection and persistent abnormal liver function tests. There are two treatment regimens that are primarily used to treat hepatitis C: monotherapy (using an interferon agent – either a "conventional" or longer-acting pegylated interferon) and combination therapy (using an interferon agent and ribavirin). Interferon, which is injected into the bloodstream, works by bolstering the



(A) (As)

[0074] Bases may include, for example, potassium hydroxide, sodium hydroxide and any other suitable base. In embodiments, the base is potassium hydroxide. In embodiments, the base is sodium hydroxide. Solvents may include, for example, dimethyl sulfoxide, 2-propanol, water, and any other suitable solvent or mixtures thereof. In an embodiment, compound **(A)** is reacted with sodium hydroxide in a mixture of dimethyl sulfoxide, 2-propanol and water to give compound (**As**) as the sodium salt. In an embodiment the conversion to the corresponding salt is conducted at a temperature of about 68 °C.

[0075] Organic salts of compound **(A)** may be made from amines, such as tromethamine, diethylamine, *N*,*N*'-dibenzylethylenediamine, chloroprocaine, choline, diethanolamine, ethylenediamine, meglumine (*N*-methylglucamine), and procaine. Basic nitrogen-containing groups can be quaternized with agents such as lower alkyl (C_1-C_6) halides (*e.g.*, methyl, ethyl, propyl, and butyl chlorides, bromides, and iodides), dialkyl sulfates (*e.g.*, dimethyl, diethyl, dibutyl, and diamyl sulfates), long chain halides (*e.g.*, decyl, lauryl, myristyl, and stearyl chlorides, bromides, and iodides), arylalkyl halides (*e.g.*, benzyl and phenethyl bromides), and others.

[0076] The disclosure is also directed to particular salts and polymorphs of certain disclosed compounds, including intermediates of the disclosed processes, as well as compositions comprising and processes for preparing such compounds, salts, and polymorphs. For example, this disclosure is directed, in part, to crystalline forms of *N*-(6-(3-*tert*-butyl-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2-methoxyphenyl)naphthalen-2-yl)methanesulfonamide (compound **(A)**) and the corresponding sodium and potassium salts, namely the solvate, hydrate, and solvent-free crystalline forms described in International Patent Publication Nos. WO 2009/039134 and WO2009/039127 ~~which are incorporated herein by reference~~.

B. Process for Preparing 6-(3-*tert*-butyl-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2-methoxyphenyl)naphthalen-2-yl 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate *(compound 5)*.

[0077] Compound **(5)** may be prepared by reacting 1-(3-*tert*-butyl-5-(6-hydroxynaphthalen-2-yl)-4-methoxyphenyl)pyrimidine-2,4(1*H*,3*H*)-dione (compound **(4)**) with a sulfonyl fluoride, sulfonyl chloride, or sulfonic acid anhydride, wherein X^1 is chlorine or fluorine, and R^{1a} is *p*-tolyl, phenyl, methyl, ethyl,

bromo-5-*tert*-butyl-4-methoxyphenyl)pyrimidine-2,4(1*H*,3*H*)-dione (compound (**1b**)), or 1-(3-*tert*-butyl-5-iodo-4-methoxyphenyl)pyrimidine-2,4(1*H*,3*H*)-dione (compound (**1c**)). The preparation of compound **(1)** is described in Example 1 below as well as in International Patent Publication No. WO 2009/039127 ~~which is incorporated herein by reference~~.

[0085] Y^1 of compound **(3)** may be a boronic acid, borate ester, or borate salt. In embodiments, Y^1 is a boronic acid. In embodiments, Y^1 is a borate ester. In embodiments, Y^1 is a borate salt. Compound **(3)** may include, for example, 6-hydroxynaphthalen-2-ylboronic acid (compound (**3a**)), potassium trifluoro(6-hydroxynaphthalen-2-yl)borate (compound (**3b**)), and 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)naphthalen-2-ol (compound (**3c**)), each of which are commercially available.

[0086] The cross-coupling reaction may be conducted in the presence of catalyst precursor. The catalyst may be, for example, a silicon, boron, tin, zinc or any other suitable catalyst. In embodiments, the catalyst is a transition metal catalyst precursor. In embodiments, the transition metal catalyst precursor is a palladium catalyst precursor. Palladium catalyst precursors may include, for example, tetrakis(triphenylphosphine)palladium(0), dichlorobis(triphenylphosphine)palladium(II), tris(dibenzylidineacetone)dipalladium(0), palladium(II) diacetate, dichlorobis(triphenylphosphine)palladium, [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane, or any other suitable palladium catalyst precursor. In embodiments, the palladium catalyst precursor is tetrakis(triphenylphosphine)palladium(0). In embodiments, the palladium catalyst precursor is dichlorobis(triphenylphosphine)palladium(II). In embodiments, the palladium catalyst precursor is tris(dibenzylidineacetone)dipalladium(0). In embodiments, the palladium catalyst precursor is palladium(II) diacetate. In embodiments, the palladium catalyst precursor is dichlorobis(triphenylphosphine)palladium. In embodiments, the palladium catalyst precursor is [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane.

[0087] The cross-coupling reaction may be conducted in the presence of a ligand. In embodiments the ligand is a phosphine. Ligands may include, for example, tri-*t*-butylphosphine, tricylcohexylphosphine, tris(2-furyl)phosphine, 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, 1,3,5,7-tetramethyl-8-phenyl-2,4,6-trioxa-8-phosphatricyclo[3.3.1.1^{3,7}]decane, biphenyl-2-yldicyclohexylphosphine, dicyclohexyl(2',6'-dimethoxybiphenyl-2-yl)phosphine, dicyclohexyl(2',4',6'-triisopropylbiphenyl-2-yl)phosphine, or any other suitable ligand. In embodiments, the ligand is tri-*t*-butylphosphine. In embodiments, the ligand is tricylcohexylphosphine. In embodiments, the ligand is, tris(2-furyl)phosphine. In embodiments, the ligand is 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl. In embodiments, the ligand is 1,3,5,7-tetramethyl-8-phenyl-2,4,6-trioxa-8-phosphatricyclo[3.3.1.1^{3,7}]decane. In embodiments, the ligand is biphenyl-2-yldicyclohexylphosphine. In embodiments, the ligand is dicyclohexyl(2',6'-dimethoxybiphenyl-2-yl)phosphine. In embodiments, the ligand is dicyclohexyl(2',4',6'-triisopropylbiphenyl-2-yl)phosphine.

[0088] Compound **(1)** may be reacted with compound **(3)** in the presence of a base. Bases may include,

temperature at 68 °C. Antisolvent solution (354 g) was added to the reactor over 7 hours while maintaining the internal temperature at 68 °C. The contents of the reactor were cooled to an internal temperature of 0 °C over 7 hours and then mixed at 0 °C for 7 hours. The solids were isolated by filtration and washed with 252 g of the chilled wash solution. The isolated solids were dried in a vacuum oven at 50 °C for 19 hours. The title compound was isolated as a white solid (30.7 g, 92% potency vs. free acid standard, 57.2 mmol free acid equivalent, 88% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.75 (s, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.59 (dd, J = 8.8, 2.2 Hz, 2H), 7.45 (dd, J = 8.5, 1.8 Hz, 1H), 7.27 (d, J = 2.6 Hz, 2H), 7.21 (d, J = 2.7 Hz, 1H), 7.06 (dd, J = 8.8, 2.2 Hz, 1H), 5.62 (d, J = 7.8 Hz, 1H), 3.24 (s, 3H), 2.68 (s, 3H), 1.40 (s, 9H).

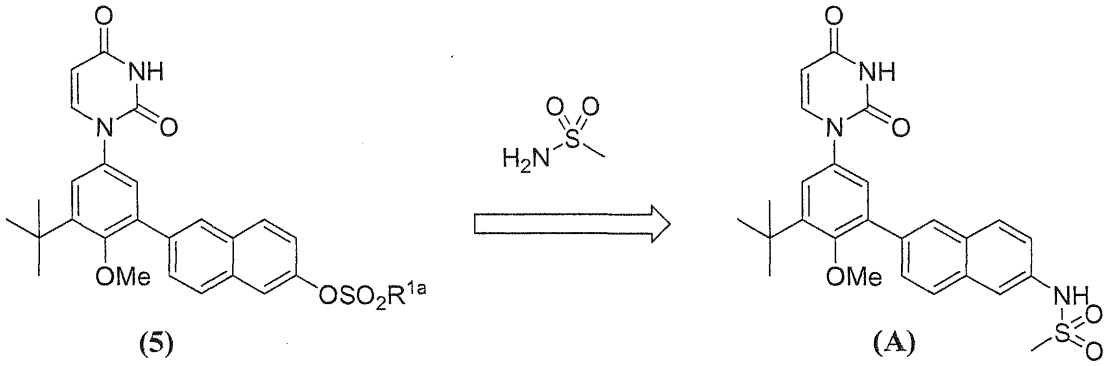
[00195] Overall, the process demonstrated in this application provides the desired product with a cleaner impurity profile than the previously disclosed process (International Patent Publication No. WO 2009/039127) both in terms of gross impurities and trace impurities that were of concern for their genotoxic potential.

[00196] ~~All references (patent and non-patent) cited above are incorporated by reference into this patent application.~~ The discussion of all those references (patent and non-patent) cited above is intended merely to summarize assertions made by their authors. No admission is made that any reference (or a portion of a reference) is relevant prior art (or prior art at all). Applicants reserve the right to challenge the accuracy and pertinence of the cited references.

WE CLAIM:

1. A process for preparing *N*-(6-(3-*tert*-butyl-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2-methoxyphenyl)naphthalen-2-yl)methanesulfonamide (compound **(A)**) or a salt thereof, wherein the process comprises:

sulfonamidating compound (**5**):



(5) **(A)**

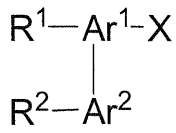
wherein R^{1a} is selected from the group consisting of *p*-tolyl, phenyl, methyl, ethyl, trifluoromethyl, perfluorobutyl, perfluoropentyl, perfluorohexyl, perfluorooctyl and isomers and homologs thereof.

2. The process of claim **1**, wherein R^{1a} is perfluorobutyl.

3. The process of claim **1**, wherein compound **(5)** is sulfonamidated using a transition metal catalyst precursor and ligand.

4. The process of claim **3**, wherein the ligand is a phosphine.

5. The process of claim **4**, wherein the phosphine ligand is a ligand of formula (**I**)



(I)

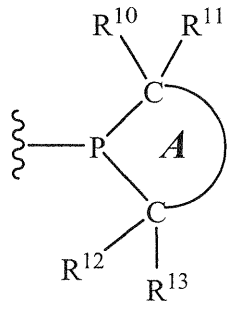
or a salt therof,

wherein

Ar^1 and Ar^2 are each independently aryl or heteroaryl, and wherein Ar^1 and Ar^2 are each independently optionally substituted with one or more R^1 and R^2, respectively;

R^1 and R^2 are independently selected at each occurrence from the group consisting of hydrogen; amino; hydroxyl; cyano; halo; alkyl; alkenyl; alkynyl; haloalkyl; haloalkoxy; oxoalkyl; alkoxy; alkylamino; dialkylamino; cycloalkyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; cycloalkyloxy optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; 5- or 6-membered heteroaryl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; phenyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; hydroxyalkyl; hydroxyalkoxy; alkoxyalkyl; aminoalkyl; *N*-alkylaminoalkyl; *N*,*N*-dialkylaminoalkyl; *N*,*N*,*N*-trialkylammoniumalkyl; L^1–C(O)–$OR^{1'}$, L^1–P(O)-$(OR^{1'})_2$, or L^1–$S(O)_2$–$OR^{1'}$, wherein L^1 is a bond or alkylene, and $R^{1'}$ is selected from the group consisting of hydrogen, alkyl and hydroxyalkyl; L^2–O–C(O)–$R^{2'}$, wherein L^2 is a bond or alkylene, and $R^{2'}$ is alkyl or hydroxyalkyl; L^3–C(O)–$NR^{3'}R^{4'}$, wherein L^3 is a bond or alkylene, and $R^{3'}$ and $R^{4'}$ are each independently selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl; L^4–$NR^{5'}$–C(O)–$R^{6'}$, wherein L^4 is a bond or alkylene, $R^{5'}$ is hydrogen or alkyl, and $R^{6'}$ is alkyl or hydroxyalkyl; sulfamoyl; *N*-(alkyl)sulfamoyl; *N*,*N*-(dialkyl)sulfamoyl; sulfonamide; sulfate; alkylthio; thioalkyl; and a ring containing an alkylene or –O–$(CH_2)_m$–O– formed by the joining together of any two R^1 or any two R^2 or an R^1 and an R^2 , wherein m is 1, 2, 3 or 4;

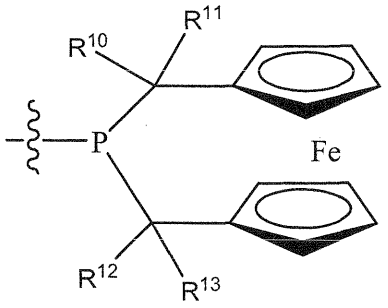
X is a phosphine of formula (Ia):



(Ia)

wherein ring *A* is a monocyclic heterocyclic ring, bicyclic heterocyclic ring, or tricyclic heterocyclic ring, and wherein ring *A* includes 0 to 9 ring atoms in addition to the phosphorus and 2 carbon ring atoms of formula (Ia), wherein said ring atoms are each independently selected from the group consisting of carbon, oxygen, nitrogen and sulfur; or

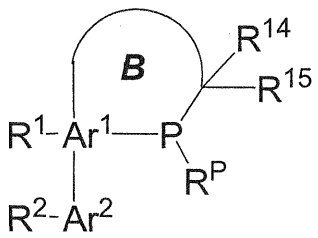
X is a phosphine of formula (Ib):



; or

(Ib)

X is a phosphine fused to Ar^1 to give a compound of formula (Ic):



(Ic)

wherein, ring ***B*** is a phosphorus heterocyclic ring with 0 to 5 ring atoms in addition to the phosphorous and carbon ring atoms of formula (I-c), wherein said ring atoms are each independently selected from the group consisting of carbon, oxygen, nitrogen and sulfur, and

wherein the ring atoms of ring ***A*** and ring ***B*** are each independently optionally substituted with one or more substituents selected from the group consisting of alkenyl; alkoxy; alkoxyalkyl; alkyl; alkylamino; alkylthio; alkynyl; aminoalkyl; *N*-alkylaminoalkyl; *N*,*N*-dialkylaminoalkyl; *N*,*N*,*N*-trialkylammoniumalkyl; arylalkyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; cycloalkyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; dialkylamino; halo; haloalkyl; fluoroalkyl; $C_{5\text{-}6}$ heteroaryl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; heterocycloalkyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; hydroxy; hydroxyalkyl; oxo; an exocyclic double bond optionally substituted with alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl, or heteroaryl; a 3- to 7-membered spiro ring containing zero, one, or two heteroatoms; phenyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; L^1-C(O)–$OR^{1'}$, L^1-P(O)-$(OR^{1'})_2$, or L^1–$S(O)_2$–$OR^{1'}$, wherein L^1 is a bond or alkylene, and $R^{1'}$ is selected from the group consisting of hydrogen, alkyl or hydroxyalkyl; L^2–O–C(O)–$R^{2'}$, wherein L^2 is a bond or alkylene, and $R^{2'}$ is alkyl or hydroxyalkyl; L^3–C(O)–$NR^{3'}R^{4'}$, wherein L^3 is a bond or alkylene, and $R^{3'}$ and $R^{4'}$ are each independently selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl; L^4–$NR^{5'}$–C(O)–$R^{6'}$, wherein L^4 is a bond or alkylene, $R^{5'}$ is hydrogen or alkyl, and $R^{6'}$ is alkyl or hydroxyalkyl; and L^7–$NR^{8'}$–$S(O)_2$–$R^{9'}$, wherein L^7 is a bond or alkylene, $R^{8'}$ is hydrogen or alkyl, and $R^{9'}$ is alkyl or hydroxyalkyl;

R^P is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and heteroaryl, wherein R^P is optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; or R^P is a bridging group between the phosphorus and another ***B*** ring atom, wherein R^P is selected from the group consisting of alkylene, alkenylene, alkynylene, and –$(CR^{41}R^{42}–O)_q$–, wherein R^{41} and R^{42} are each independently hydrogen or alkyl, and wherein q is 1 or 2, and wherein R^P is optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy;

as to R^{10}, R^{11}, R^{12}, and R^{13},

i. R^{10} or R^{11} together with R^{12} or R^{13} form a ring; or

ii. R^{10} and R^{11} together with the carbon atom to which they are attached form a spirocyclic ring and/or R^{12} and R^{13} together with the carbon atom to which they are attached form a spirocyclic ring; or

iii. one or more of R^{10}, R^{11}, R^{12} and R^{13} form a ring together with a ring substituent of ring ***A***; or

iv. at least one of substituents R^{10}, R^{11}, R^{12} and R^{13} do not form a ring, said substituents are each independently selected from the group consisting of hydrogen; alkyl; alkenyl; haloalkyl; alkynyl; oxoalkyl; cycloalkyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; heterocyclyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; C_{5-6} heteroaryl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; phenyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; hydroxyalkyl; alkoxyalkyl; aminoalkyl; *N*-alkylaminoalkyl; *N*,*N*-dialkylaminoalkyl; *N*,*N*,*N*-trialkylammoniumalkyl; thioalkyl; L^{13}–C(O)–$OR^{14'}$, L^{13}–P(O)–$(OR^{14'})_2$, or L^{13}–$S(O)_2$–$OR^{14'}$, wherein L^{13} is a bond or alkylene, and $R^{14'}$ is selected from the group consisting of hydrogen, alkyl and hydroxyalkyl; L^{15}–O–C(O)–$R^{16'}$, wherein L^{15} is alkylene and $R^{16'}$ is alkyl or hydroxyalkyl; L^{17}–C(O)–$NR^{18'}R^{19'}$, wherein L^{17} is a bond or alkylene, and $R^{18'}$ and $R^{19'}$ are each independently selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl ; and L^{20}–$NR^{21'}$–C(O)–$R^{22'}$, wherein L^{20} is alkylene, $R^{21'}$ is hydrogen or alkyl, and $R^{22'}$ is alkyl or hydroxyalkyl; and

as to R^{14} and R^{15},

R^{14} and R^{15} together with the carbon atom to which they are attached form a spirocyclic ring; or

one or more of R^{14} and R^{15} form a ring together with a ring atom or ring substituent of ring ***B***,

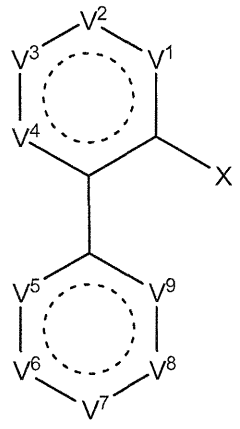
wherein, if any of substituents R^{14} and R^{15} do not form a ring, said substituents are each independently selected from the group consisting of hydrogen; alkyl; alkenyl; haloalkyl; alkynyl;

oxoalkyl; cycloalkyl optionally substituted with alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl, or heteroaryl; heterocyclyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; C_{5-6} heteroaryl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; phenyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; hydroxyalkyl; alkoxyalkyl; aminoalkyl; *N*-alkylaminoalkyl; *N,N*-dialkylaminoalkyl; *N,N,N*-trialkylammoniumalkyl; thioalkyl; L^{13}–C(O)–$OR^{14'}$, L^{13}–P(O)–$(OR^{14'})_2$, or L^{13}–$S(O)_2$–$OR^{14'}$ wherein L^{13} is a bond or alkylene, and $R^{14'}$ is selected from the group consisting of hydrogen, alkyl and hydroxyalkyl; L^{15}–O–C(O)–$R^{16'}$ wherein L^{15} is alkylene, and $R^{16'}$ is alkyl or hydroxyalkyl; L^{17}–C(O)–$NR^{18'}R^{19'}$, wherein L^{17} is a bond or alkylene and $R^{18'}$ and $R^{19'}$ are each independently selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl; and L^{20}–$NR^{21'}$–C(O)–$R^{22'}$, wherein L^{20} is alkylene, $R^{21'}$ is hydrogen or alkyl, and $R^{22'}$ is alkyl or hydroxyalkyl.

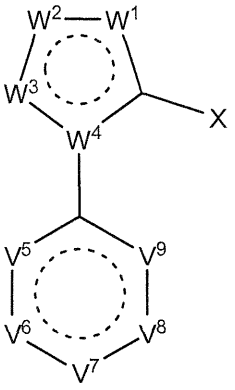
6. The process of claim **5**, wherein the ligand is selected from the group consisting of 7,7,9,9-tetramethyl-8-(2',4',6'-triisopropylbiphenyl-2-yl)-1,4-dioxa-8-phosphaspiro[4.5]decane; 2,2,6,6-tetramethyl-1-(2',4',6'-triisopropylbiphenyl-2-yl)phosphinane; 8,8,10,10-tetramethyl-9-(2',4',6'-triisopropylbiphenyl-2-yl)-1,5-dioxa-9-phosphaspiro[5.5]undecane; 2,2,6,6-tetramethyl-1-(2',4',6'-triisopropylbiphenyl-2-yl)phosphinan-4-ol; 8-(2',6'-diisopropoxybiphenyl-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane; 1,3,5,7-tetramethyl-8-(2',4',6'-triisopropylbiphenyl-2-yl)-2,4,6-trioxa-8-phosphatricyclo[3.3.1.$1^{3,7}$]decane; 2,2,6,6-tetramethyl-1-(2',4',6'-triisopropyl-3,4,5,6-tetramethylbiphenyl-2-yl)phosphinane; 8-(2',6'-dimethoxybiphenyl-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane; 6-methoxy-*N,N*-dimethyl-2'-(7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decan-8-yl)biphenyl-2-amine; 8-(2'-methoxy-1,1'-binaphthyl-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane; 8-(1,1'-binaphthyl-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane; 7,7,9,9-tetramethyl-8-(2-(naphthalen-1-yl)phenyl)-1,4-dioxa-8-phosphaspiro[4.5]decane; 7,7,9,9-tetramethyl-8-(2-(naphthalen-2-yl)phenyl)-1,4-dioxa-8-phosphaspiro[4.5]decane; 2,2,6,6-tetramethyl-1-(2',4',6'-triisopropylbiphenyl-2-yl)phosphinan-4-one; 3,3,8,8,10,10-hexamethyl-9-(2',4',6'-triisopropylbiphenyl-2-yl)-1,5-dioxa-9-phosphaspiro[5.5]undecane; 1-(2'-(dimethylamino)-6'-methoxybiphenyl-2-yl)-2,2,6,6-

tetramethylphosphinan-4-one; 1-(2',6'-bis(dimethylamino)biphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(2',6'-dimethoxybiphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(2',6'-diisopropoxybiphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(2'-(dimethylamino)biphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(biphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(1,1'-binaphthyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(2'-methoxy-1,1'-binaphthyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(3,6-dimethoxybiphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(3,6-dimethoxy-2',4',6'-trimethylbiphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 2,2,6,6-tetramethyl-1-(2',4',6'-triisopropyl-3,6-dimethoxybiphenyl-2-yl)phosphinan-4-one; 2,2,6,6-tetramethyl-1-(2',4',6'-triisopropyl-4,5-dimethoxybiphenyl-2-yl)phosphinan-4-one; 1-(3',5'-dimethoxybiphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(4'-*tert*-butylbiphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; N^2,N^2,N^6,N^6-tetramethyl-2'-(7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decan-8-yl)biphenyl-2,6-diamine;*N*,*N*-dimethyl-2'-(7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decan-8-yl)biphenyl-2-amine; 8-(biphenyl-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane; 8-(3,6-dimethoxybiphenyl-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane; 7,7,9,9-tetramethyl-8-(2',4',6'-triisopropyl-3,6-dimethoxybiphenyl-2-yl)-1,4-dioxa-8-phosphaspiro[4.5]decane; 8-(2-(2-methoxynaphthalen-1-yl)phenyl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane;and 8-(3,6-dimethoxy-2',4',6'-trimethylbiphenyl-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane.

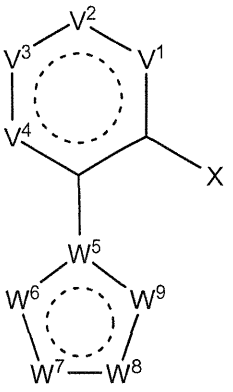
7. The process of claim **5**, wherein said phosphine ligand has a structure corresponding to a structure of a formula selected from the group consisting of formulae (I-1) - (I-42),



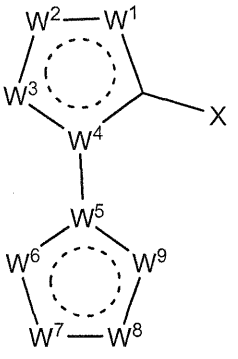
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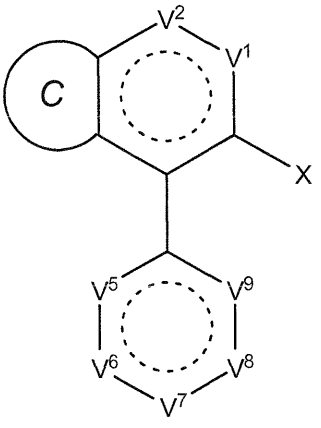
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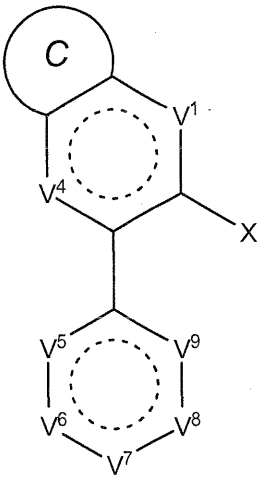
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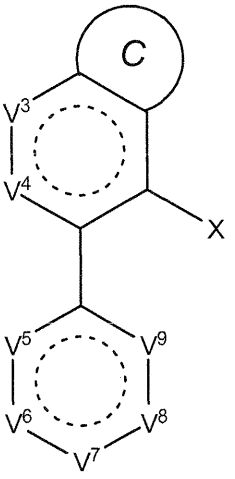
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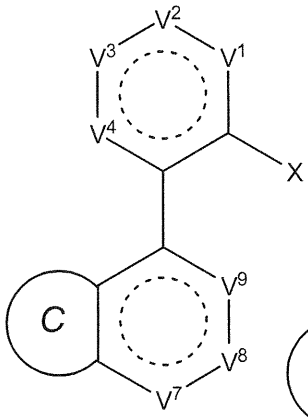
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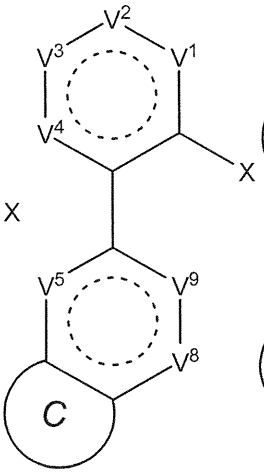
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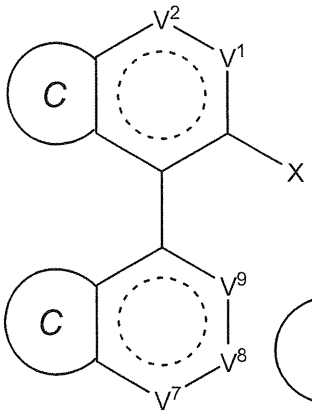
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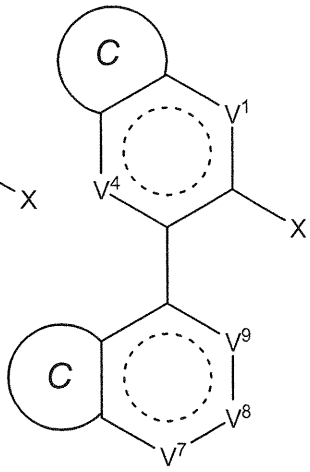
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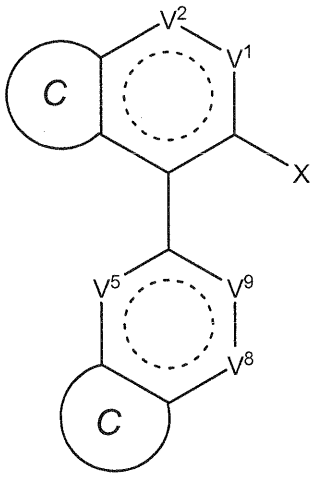
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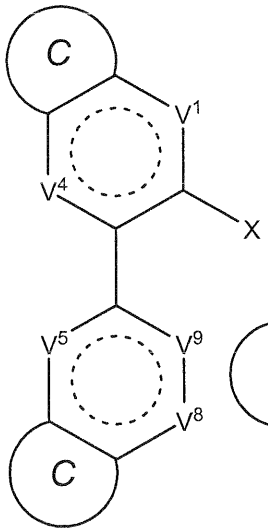
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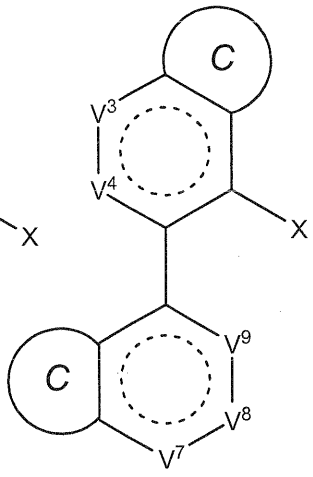
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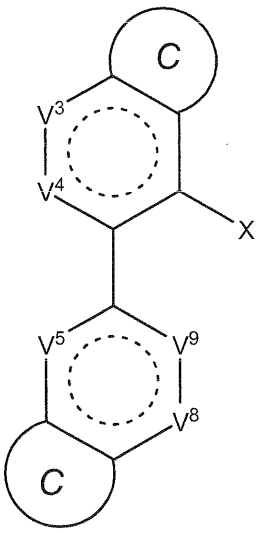
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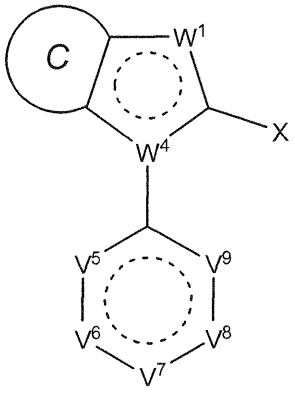
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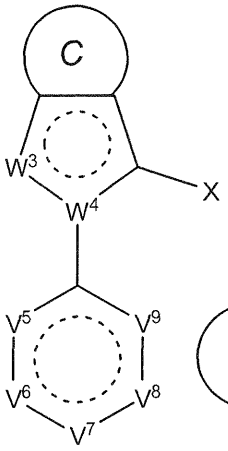
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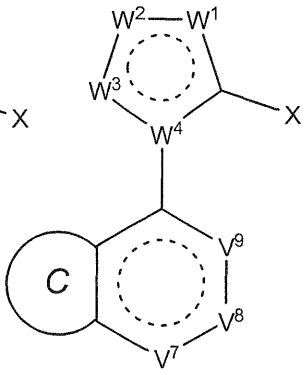
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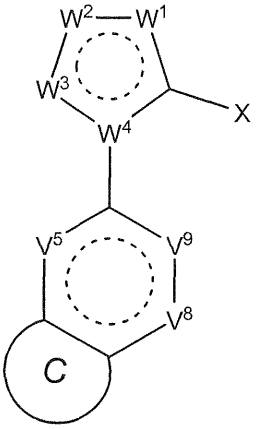
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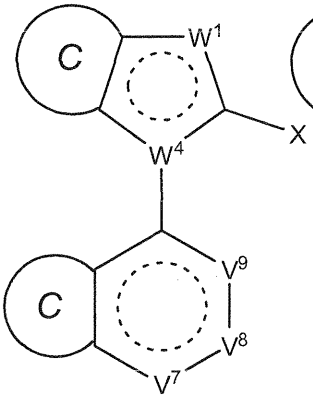
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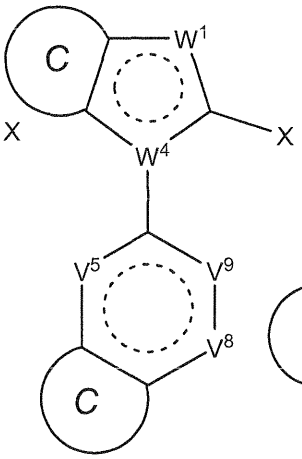
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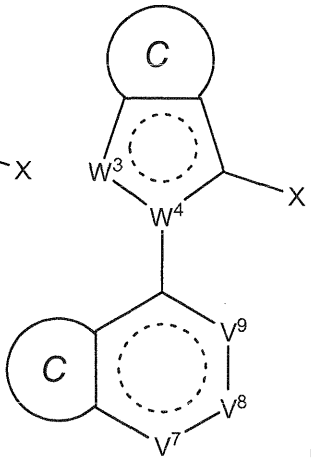
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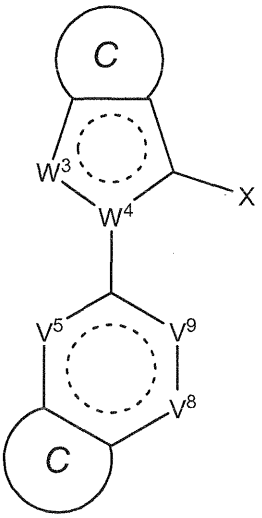
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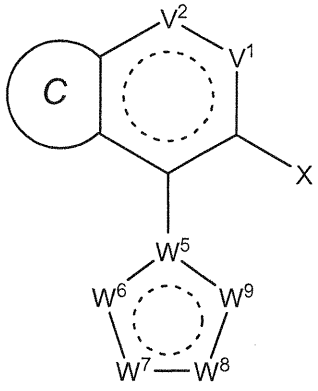
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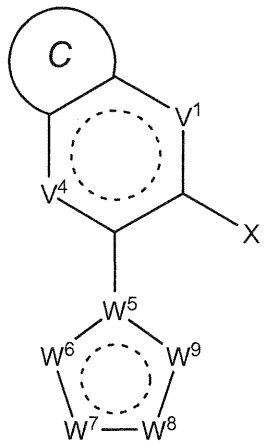
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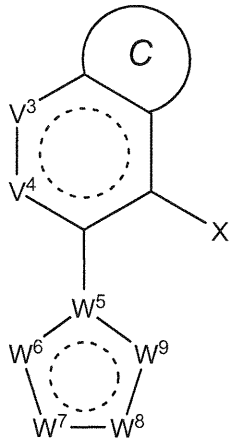
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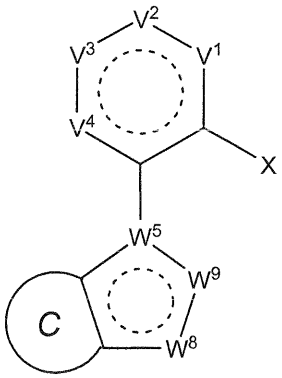
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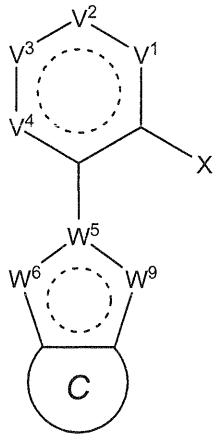
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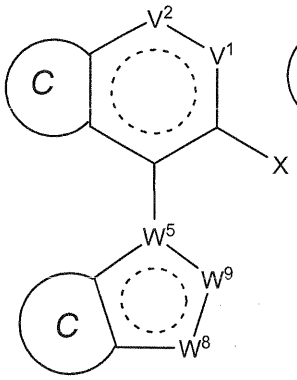
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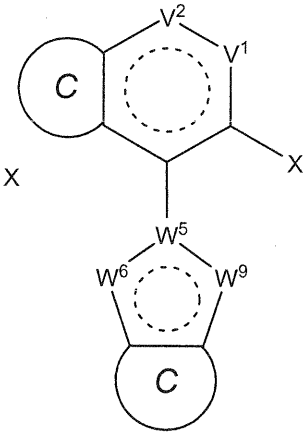
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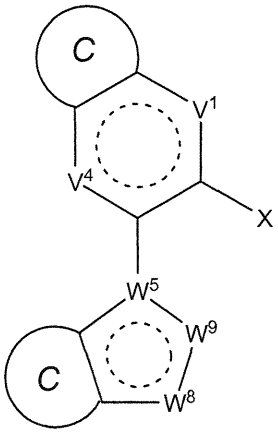
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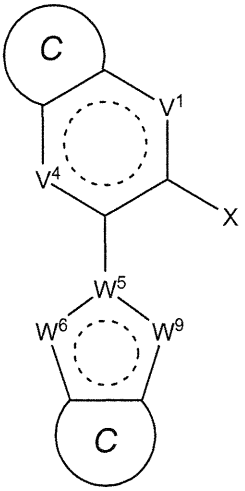
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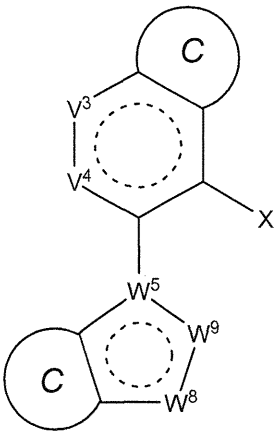
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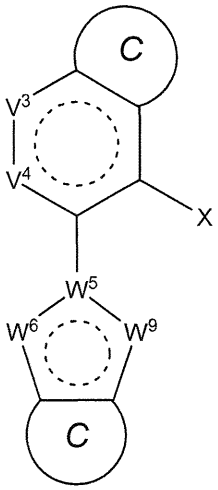
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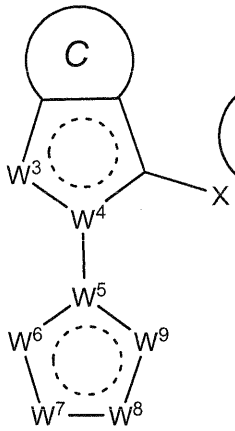
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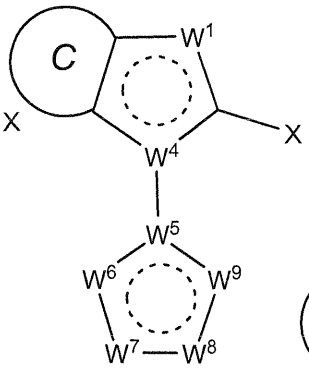
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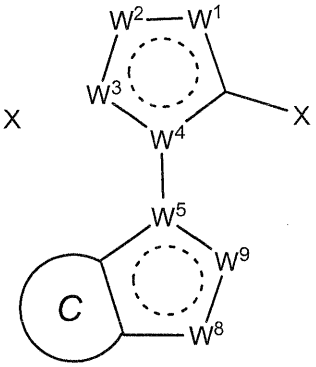
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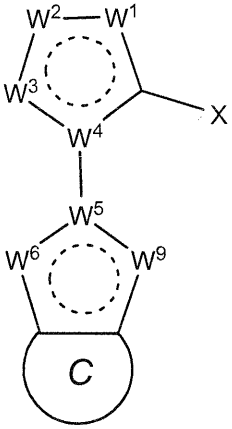
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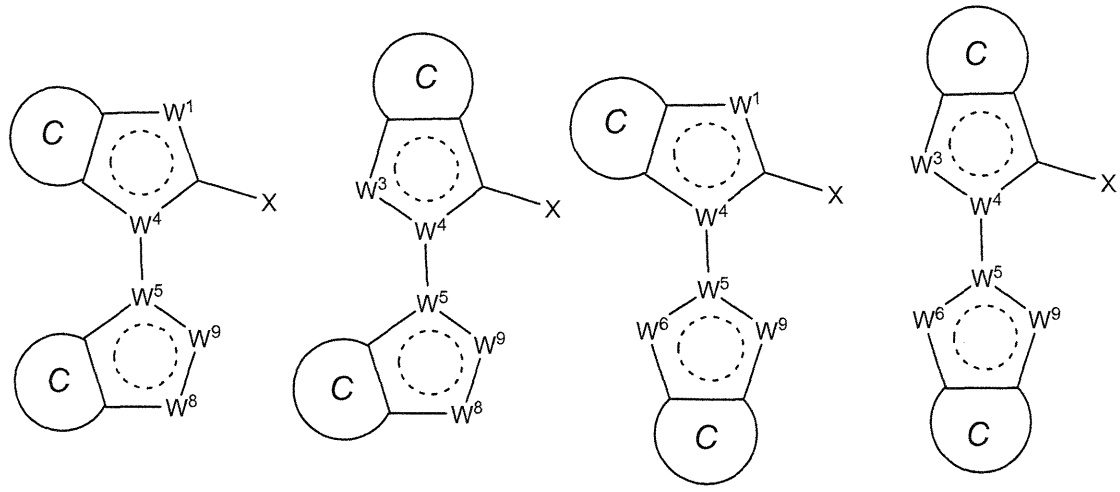
(I-36)



(I-37)



(I-38)



(I-39) (I-40) (I-41) (I-42)

or a salt thereof, wherein

X is a phosphine of formula (Ia) or (Ib);

V^1, V^2, V^3, and V^4 are each independently CR^1 or N;

V^5, V^6, V^7, V^8 and V^9 are each independently CR^2 or N;

W^1, W^2, an W^3 are each independently selected from the group consisting of CR^1, NR^1, N and O;

W^4 is C or N;

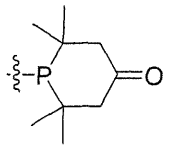
W^5 is C or N;

W^6, W^7, W^8 and W^9 are each independently selected from the group consisting of CR^2, NR^2, N and O;

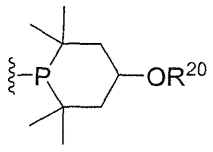
and

ring ***C***, at each occurrence, is a fused-aryl or fused-heteroaryl and is optionally substituted with R^1 and R^2.

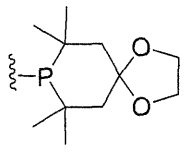
8. The process of claim **5**, wherein X is a phosphine having a structure corresponding to a formula selected from the group consisting of:



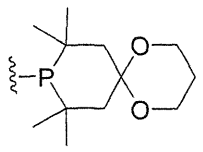
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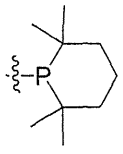
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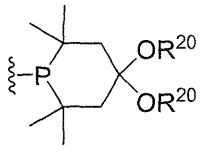
1-3



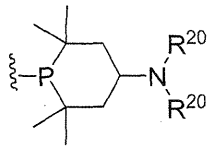
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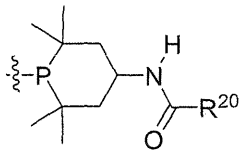
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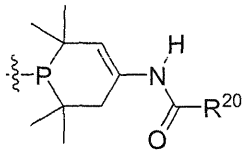
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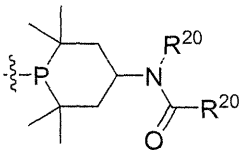
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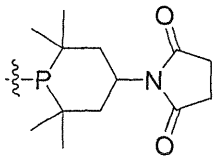
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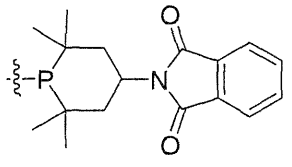
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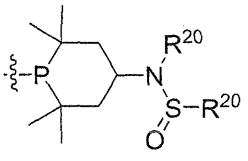
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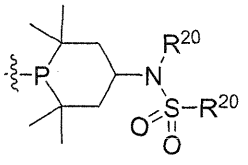
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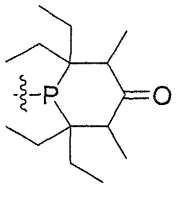
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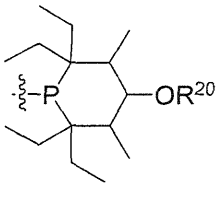
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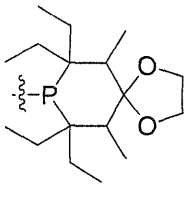
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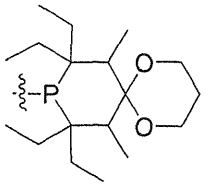
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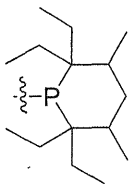
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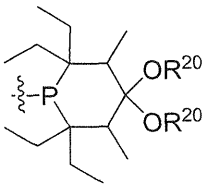
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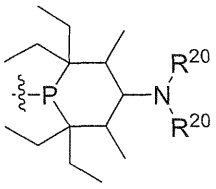
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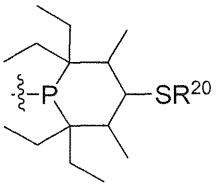
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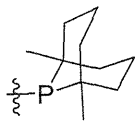
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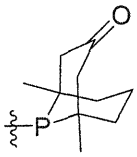
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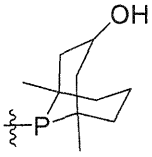
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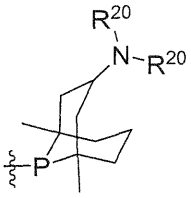
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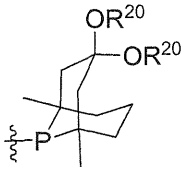
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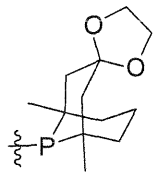
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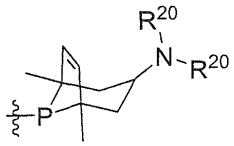
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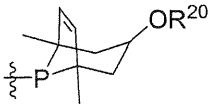
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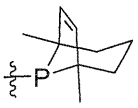
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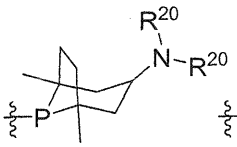
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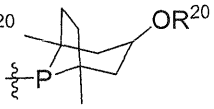
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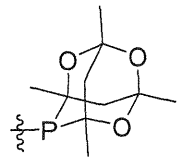
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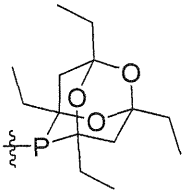
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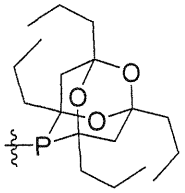
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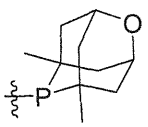
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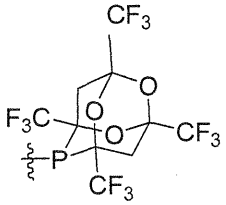
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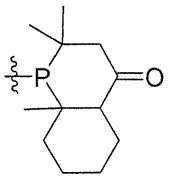
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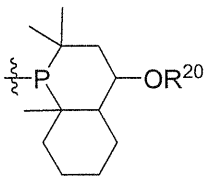
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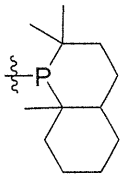
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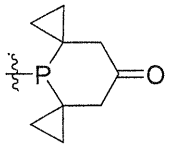
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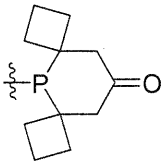
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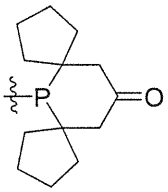
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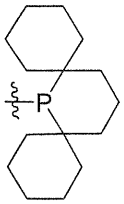
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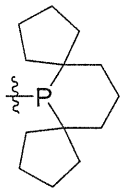
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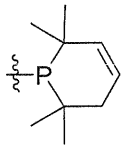
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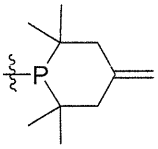
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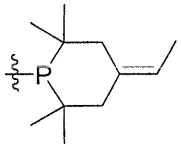
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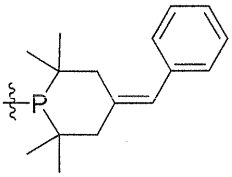
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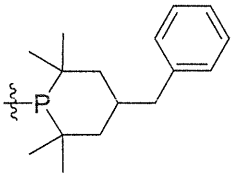
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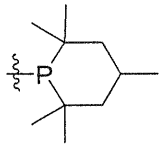
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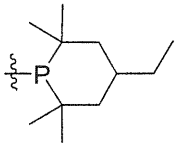
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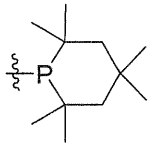
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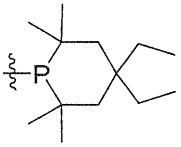
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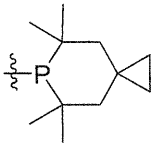
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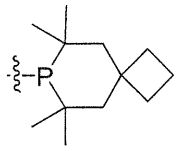
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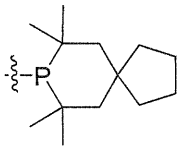
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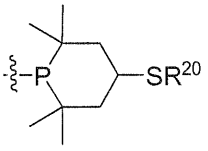
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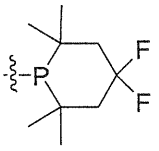
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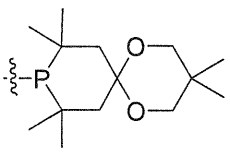
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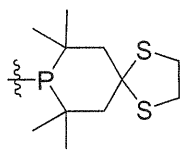
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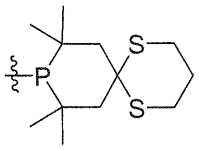


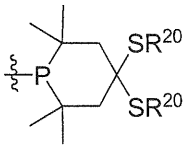
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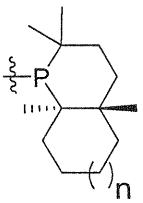


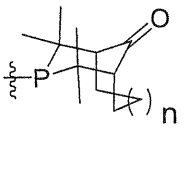
1-64



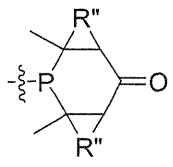








1-65 1-66 1-67 1-68 1-69, and



,

1-70

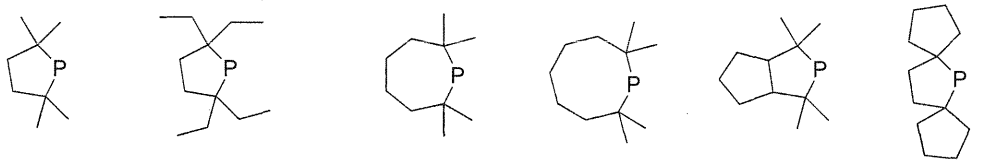
or a salt thereof, wherein

R" is selected from the group consisting of oxygen, NR^{20}, and $C(R^{20})_2$;

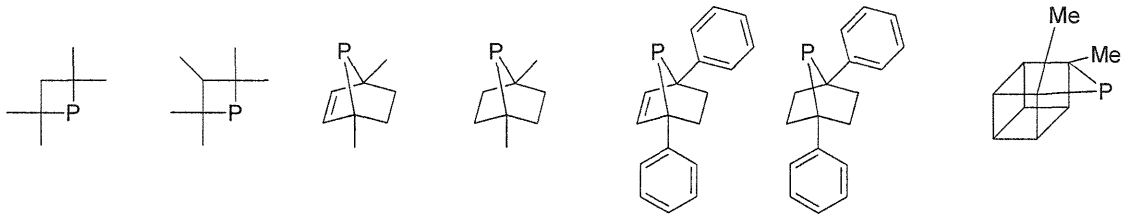
R^{20} is hydrogen or alkyl; and

n is 0, 1, or 2.

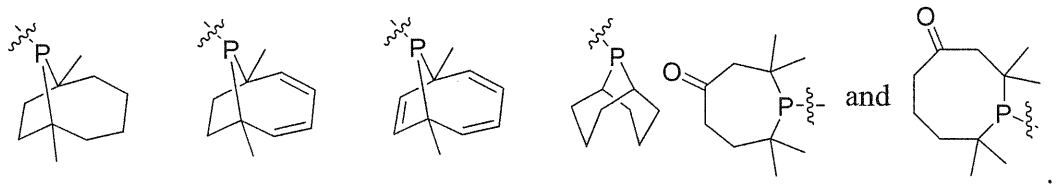
9. The process of claim **5**, wherein X is a phosphine having a structure corresponding to a formula selected from the group consisting of



2-1 2-2 2-3 2-4 2-5 2-6



2-7 2-8 2-9 2-10 2-11 2-12 2-13



2-14 2-15 2-16 2-17 2-18 2-19

10. The process of claim **3**, wherein the transition metal catalyst precursor is a palladium catalyst precursor.

11. The process of claim **10**, wherein the palladium catalyst precursor is selected from the group consisting of tetrakis(triphenylphosphine)palladium(0), dichlorobis(tri-*o*-tolylphosphine)palladium(II), palladium(II) acetate, [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), tris(dibenzylideneacetone)dipalladium(0), dichloro(dibenzylideneacetone)dipalladium(II), dichlorotris(cyclohexylphosphine) palladium(II), dichlorobis(triphenyl-phosphine) palladium(II), chloro(η3-allyl)palladium(II) dimer-triphenylphosphine, palladium(II) chloride, palladium(II) bromide, and bis(acetonitrile)dichloropalladium(II).

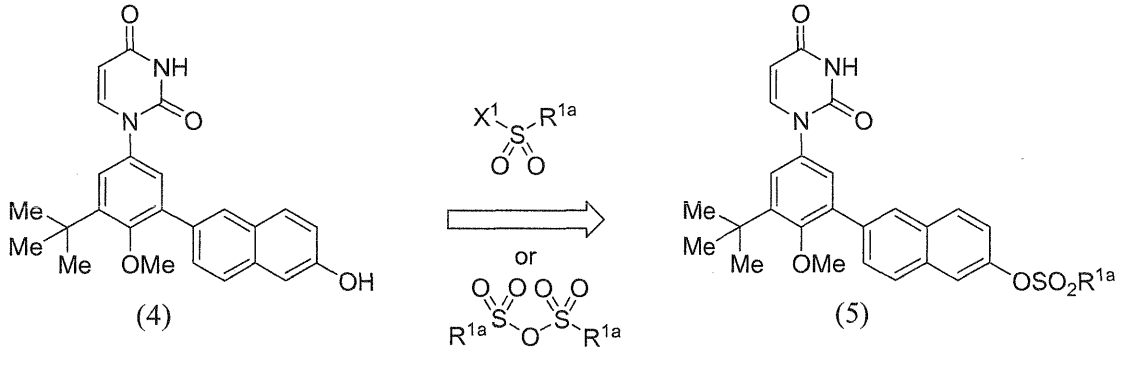
12. The process of any one of claims **1-11**, wherein compound **(5)** is sulfonamidated in the presence of a base.

13. The process of claim **12**, wherein the base is selected from the group consisting of potassium phosphate tribasic, cesium carbonate, potassium carbonate, sodium carbonate, sodium *tert*-butoxide, potassium *tert*-butoxide, lithium bis(trimethylsilyl)amide, and lithium diisopropylamide.

14. The process of any one of claims **1-13**, wherein compound **(5)** is sulfonamidated in the presence of solvent.

15. The process of claim **14**, wherein the solvent is selected from the group consisting of tetrahydrofuran, *N*,*N*-dimethylformamide, *N*,*N*-dimethylacetamide, *N*-methyl- pyrrolidone, dimethyl sulfoxide, 1,2-dimethoxyethane, 1,4-dioxane, acetonitrile, cyclopentyl methyl ether, toluene, benzene, *tert*-amyl alcohol, and *tert*-butyl alcohol.

16. The process of any one of claims **1-15**, wherein compound **(5)** is prepared by sulfonylating 1-(3-*tert*-butyl-5-(6-hydroxynaphthalen-2-yl)-4-methoxyphenyl)pyrimidine-2,4(1*H*,3*H*)-dione (compound **4**).



wherein

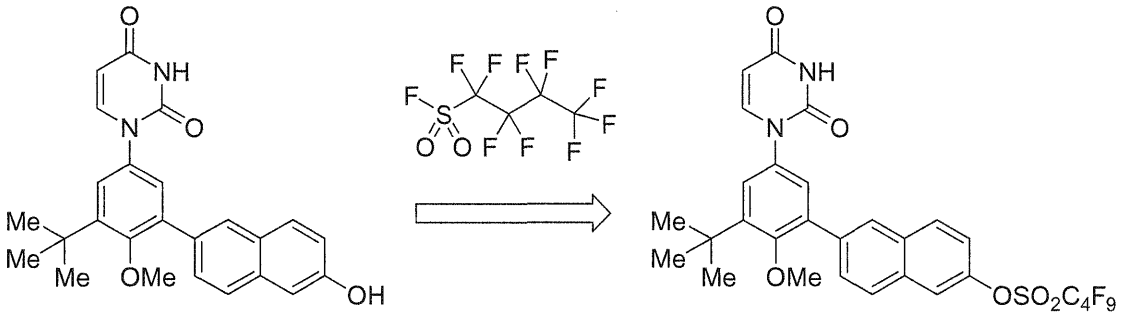
X^1 is selected from the group consisting of chlorine and fluorine; and

R^{1a} is selected from the group consisting of *p*-tolyl, phenyl, methyl, ethyl, trifluoromethyl, perfluorobutyl, perfluoropentyl, perfluorohexyl, perfluorooctyl, and isomers and homologs thereof.

17. The process of claim **16**, wherein the sulfonyl compound is perfluorobutanesulfonyl fluoride.

18. The process of any one of claims **1-17**, wherein R^{1a} is perfluorobutyl.

19. The process of claim **18**, wherein compound **(5)** is prepared by reacting 1-(3-*tert*-butyl-5-(6-hydroxynaphthalen-2-yl)-4-methoxyphenyl)pyrimidine-2,4(1*H*,3*H*)-dione (compound **4**) with perfluorobutanesulfonyl fluoride:

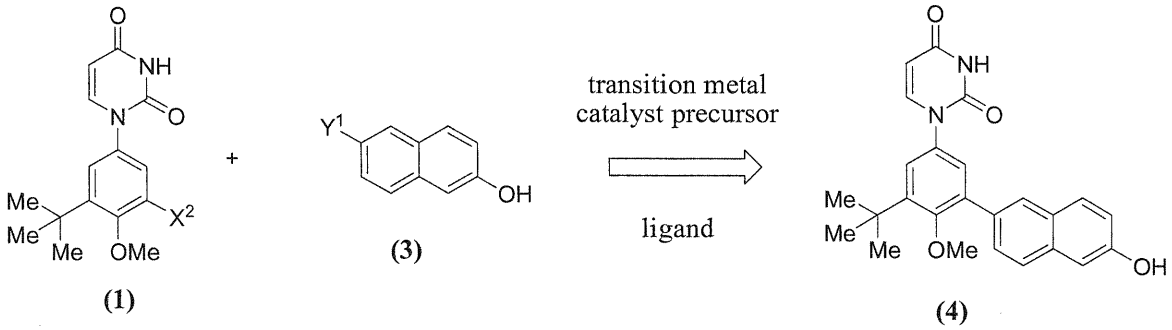


(4) **(5a)**

20. The process of claim **19**, wherein compound (**4**) and perfluorobutanesulfonyl fluoride are reacted in the presence of base.

21. The process of any one of claims **19** and **20**, wherein compound (**4**) and perfluorobutanesulfonyl fluoride are reacted in the presence of solvent.

22. The process of any one of claims **19-21**, wherein compound (**4**) is prepared by a process comprising coupling compound (**1**) with compound (**3**):



wherein

X^2 of compound **(1)** is selected from the group consisting of chlorine, bromine and iodine; and

Y^1 of compound **(3)** is selected from the group consisting of boronic acid, borate ester, and borate salt.

23. The process of claim **22**, wherein compound **(1)** is 1-(3-*tert*-butyl-5-iodo-4-methoxyphenyl)pyrimidine-2,4(1*H*,3*H*)-dione (compound (**1c**)).

24. The process of claim **22**, wherein compound **(3)** is 6-hydroxynaphthalen-2-ylboronic acid (compound (**3a**)).

25. The process of claim **22**, wherein compound **(1)** and **(3)** are coupled using a transition metal catalyst precursor and ligand.

26. The process of claim **25**, wherein the phosphine ligand is selected from the group consisting of tri-*t*-butylphosphine, tricylcohexylphosphine, tris(2-furyl)phosphine, 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, 1,3,5,7-tetramethyl-8-phenyl-2,4,6-trioxa-8-phosphatricyclo[3.3.1.$1^{3,7}$]decane, biphenyl-2-yldicyclohexylphosphine, dicyclohexyl(2',6'-dimethoxybiphenyl-2-yl)phosphine, and dicyclohexyl(2',4',6'-triisopropylbiphenyl-2-yl)phosphine.

27. The process of claim **26**, wherein the ligand is 1,3,5,7-tetramethyl-8-phenyl-2,4,6-trioxa-8-phosphatricyclo[3.3.1.13,7]decane.

28. The process claim **22**, wherein the transition metal catalyst precursor is a palladium catalyst precursor.

29. The process of claim **28**, wherein the palladium catalyst precursor is selected from the group consisting of tetrakis(triphenylphosphine)palladium(0), dichlorobis(triphenylphosphine)palladium(II), tris(dibenzylidineacetone)dipalladium, palladium(II) diacetate, dichlorobis(triphenylphosphine)palladium, and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane.

30. The process of any one of claims **22-28**, wherein compounds **(1)** and **(3)** are coupled in the presence of a base.

31. The process of claim **30**, wherein the base is selected from the group consisting of potassium phosphate tribasic, cesium carbonate, potassium carbonate, sodium carbonate, potassium *tert*-butoxide and cesium fluoride.

32. The process of any one of claims **22-31**, wherein compounds **(1)** and **(3)** are coupled in the presence of a solvent.

33. The process of claim **32**, wherein the solvent is selected from the group consisting of tetrahydrofuran, *N*,*N*-dimethylformamide, 1,2-dimethoxyethane, 1,4-dioxane, ethanol, toluene, water and mixtures thereof.

34. The process of claim **1**, wherein compound **(A)** is converted to a corresponding salt, compound (**As**).

35. The process of claim **34**, wherein compound **(A)** is converted to compound (**As**) by treatment with a base.

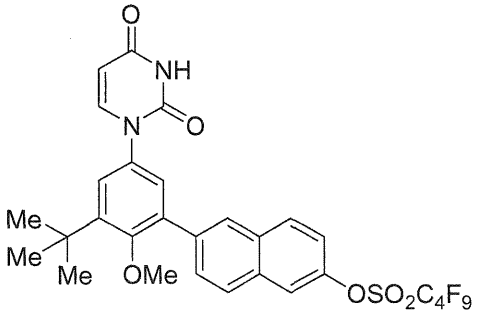
36. The process of claim **35**, wherein the base is sodium hydroxide or potassium hydroxide.

37. The process of claim **34**, wherein compound **(A)** is converted to compound (**As**) in the presence of a solvent.

38. The process of claim **37**, wherein the solvent is selected from the group consisting of dimethyl sulfoxide, 2-propanol, water and mixtures thereof.

39. The process of claim **34**, wherein compound (**As**) is a sodium salt.

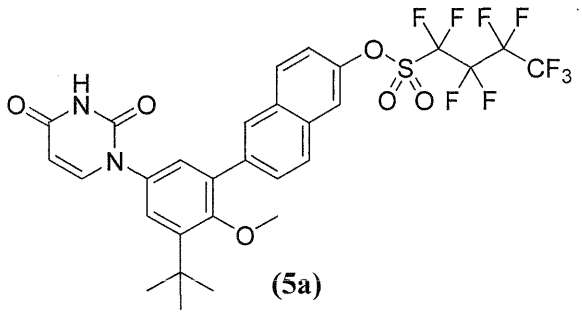
40. A compound or salt thereof, wherein the compound corresponds in structure to formula **(5a)**:



(5a)

41. The compound of claim **40**, wherein the compound is prepared by the process of any one of claims **19-21**.

42. The process of claim **1**, wherein compound **(5)** is 6-(3-tert-butyl-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2-methoxyphenyl)naphthalen-2-yl 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate (compound **5a**):



(5a)

43. The process of claim **3**, wherein the ligand is selected from the group consisting of di-*tert*-butyl(2',4',6'-triisopropyl-3,4,5,6-tetramethylbiphenyl-2-yl)phosphine; di-*tert*-butyl(2',4',6'-triisopropylbiphenyl-2-yl)phosphine; di-*tert*-butyl(2'-isopropoxy-1,1'-binaphthyl-2-yl)phosphine; 2,2,5,5-tetramethyl-1-(2',4',6'-triisopropyl-3,4,5,6-tetramethylbiphenyl-2-yl)phospholane; 2,2,7,7-tetramethyl-1-(2',4',6'-triisopropylbiphenyl-2-yl)phosphepane; 2,2,7,7-tetramethyl-1-(2',4',6'-triisopropyl-3,4,5,6-tetramethylbiphenyl-2-yl)phosphepane; 2,2,8,8-tetramethyl-1-(2',4',6'-triisopropyl-3,4,5,6-tetramethylbiphenyl-2-yl)phosphocane; 1,3,5,7-tetramethyl-8-phenyl-2,4,6-trioxa-8-phosphatricyclo[3.3.1.1^{3,7}]decane; and di-*tert*-butyl(2',4',6'-triisopropyl-3,6-dimethoxybiphenyl-2-yl)phosphine.

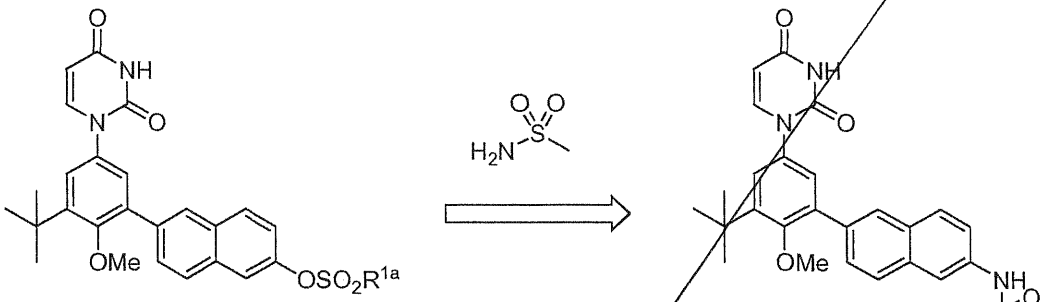
44. The process of claim **43**, wherein the ligand is di-*tert*-butyl(2',4',6'-triisopropyl-3,6-dimethoxybiphenyl-2-yl)phosphine.

45. The process of claim **3**, wherein the ligand is 7,7,9,9-tetramethyl-8-(2',4',6'-triisopropyl-3,6-dimethoxybiphenyl-2-yl)-1,4-dioxa-8-phosphaspiro[4.5]decane.

WE CLAIM:

1. A process for preparing *N*-(6-(3-*tert*-butyl-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2-methoxyphenyl)naphthalen-2-yl)methanesulfonamide (compound **(A)**) or a salt thereof, wherein the process comprises:

sulfonamidating compound **(5)**:



(5) **(A)**

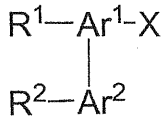
wherein R^{1a} is selected from the group consisting of *p*-tolyl, phenyl, methyl, ethyl, trifluoromethyl, perfluorobutyl, perfluoropentyl, perfluorohexyl, perfluorooctyl and isomers and homologs thereof.

2. The process of claim **1**, wherein R^{1a} is perfluorobutyl.

3. The process of claim **1**, wherein compound **(5)** is sulfonamidated using a transition metal catalyst precursor and ligand.

4. The process of claim **3**, wherein the ligand is a phosphine.

5. The process of claim **4**, wherein the phosphine ligand is a ligand of formula **(I)**



(I)

or a salt therof,

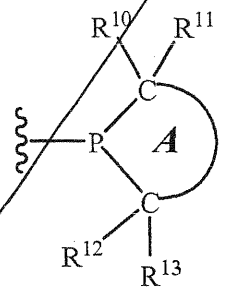
wherein

Ar^1 and Ar^2 are each independently aryl or heteroaryl, and wherein Ar^1 and Ar^2 are each independently optionally substituted with one or more R^1 and R^2, respectively;

R^1 and R^2 are independently selected at each occurrence from the group consisting of hydrogen; amino; hydroxyl; cyano; halo; alkyl; alkenyl; alkynyl; haloalkyl; haloalkoxy; oxoalkyl; alkoxy;

alkylamino; dialkylamino; cycloalkyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; cycloalkyloxy optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; 5- or 6-membered heteroaryl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; phenyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; hydroxyalkyl; hydroxyalkoxy; alkoxyalkyl; aminoalkyl; *N*-alkylaminoalkyl; *N*,*N*-dialkylaminoalkyl; *N*,*N*,*N*-trialkylammoniumalkyl; L^1–C(O)–$OR^{1'}$, L^1–P(O)-$(OR^{1'})_2$, or L^1–$S(O)_2$–$OR^{1'}$, wherein L^1 is a bond or alkylene, and $R^{1'}$ is selected from the group consisting of hydrogen, alkyl and hydroxyalkyl; L^2–O–C(O)–$R^{2'}$, wherein L^2 is a bond or alkylene, and $R^{2'}$ is alkyl or hydroxyalkyl; L^3–C(O)–$NR^{3'}R^{4'}$, wherein L^3 is a bond or alkylene, and $R^{3'}$ and $R^{4'}$ are each independently selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl; L^4–$NR^{5'}$–C(O)–$R^{6'}$, wherein L^4 is a bond or alkylene, $R^{5'}$ is hydrogen or alkyl, and $R^{6'}$ is alkyl or hydroxyalkyl; sulfamoyl; *N*-(alkyl)sulfamoyl; *N*,*N*-(dialkyl)sulfamoyl; sulfonamide; sulfate; alkylthio; thioalkyl; and a ring containing an alkylene or –O–$(CH_2)_m$–O– formed by the joining together of any two R^1 or any two R^2 or an R^1 and an R^2, wherein m is 1, 2, 3 or 4;

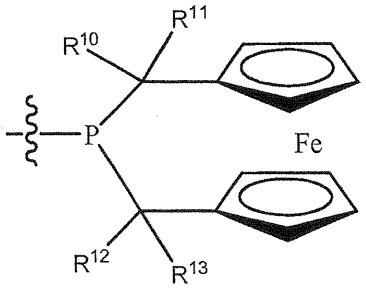
X is a phosphine of formula (Ia):



(Ia)

wherein ring *A* is a monocyclic heterocyclic ring, bicyclic heterocyclic ring, or tricyclic heterocyclic ring, and wherein ring *A* includes 0 to 9 ring atoms in addition to the phosphorus and 2 carbon ring atoms of formula (Ia), wherein said ring atoms are each independently selected from the group consisting of carbon, oxygen, nitrogen and sulfur; or

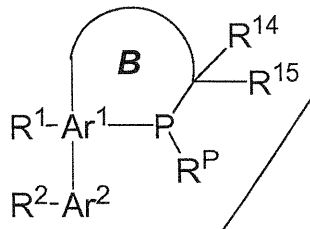
X is a phosphine of formula (Ib):



; or

(Ib)

X is a phosphine fused to Ar^1 to give a compound of formula (Ic):



(Ic)

wherein, ring ***B*** is a phosphorus heterocyclic ring with 0 to 5 ring atoms in addition to the phosphorous and carbon ring atoms of formula (I-c), wherein said ring atoms are each independently selected from the group consisting of carbon, oxygen, nitrogen and sulfur, and

wherein the ring atoms of ring ***A*** and ring ***B*** are each independently optionally substituted with one or more substituents selected from the group consisting of alkenyl; alkoxy; alkoxyalkyl; alkyl; alkylamino; alkylthio; alkynyl; aminoalkyl; *N*-alkylaminoalkyl; *N*,*N*-dialkylaminoalkyl; *N*,*N*,*N*-trialkylammoniumalkyl; arylalkyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; cycloalkyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; dialkylamino; halo; haloalkyl; fluoroalkyl; $C_{5\text{-}6}$ heteroaryl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; heterocycloalkyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; hydroxy; hydroxyalkyl; oxo; an exocyclic double bond optionally substituted with alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl, or heteroaryl; a 3- to 7-membered spiro ring containing zero, one, or two heteroatoms; phenyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; L^1-C(O)–$OR^{1'}$, L^1-P(O)-$(OR^{1'})_2$, or L^1–$S(O)_2$–$OR^{1'}$, wherein L^1 is a bond or alkylene, and $R^{1'}$ is selected from the group consisting of hydrogen, alkyl or hydroxyalkyl; L^2–O–C(O)–$R^{2'}$, wherein L^2 is a bond or alkylene, and $R^{2'}$ is alkyl or hydroxyalkyl; L^3–C(O)–$NR^{3'}R^{4'}$, wherein L^3 is a bond or alkylene, and $R^{3'}$ and $R^{4'}$ are each independently selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl; L^4–$NR^{5'}$–C(O)–$R^{6'}$, wherein L^4 is a bond or alkylene, $R^{5'}$ is hydrogen or alkyl,

and $R^{6'}$ is alkyl or hydroxyalkyl; and L^7–$NR^{8'}$–$S(O)_2$–$R^{9'}$, wherein L^7 is a bond or alkylene, $R^{8'}$ is hydrogen or alkyl, and $R^{9'}$ is alkyl or hydroxyalkyl;

R^P is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and heteroaryl, wherein R^P is optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; or R^P is a bridging group between the phosphorus and another ***B*** ring atom, wherein R^P is selected from the group consisting of alkylene, alkenylene, alkynylene, and $–(CR^{41}R^{42}–O)_q–$, wherein R^{41} and R^{42} are each independently hydrogen or alkyl, and wherein q is 1 or 2, and wherein R^P is optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy;

as to R^{10}, R^{11}, R^{12}, and R^{13},

i. R^{10} or R^{11} together with R^{12} or R^{13} form a ring; or

ii. R^{10} and R^{11} together with the carbon atom to which they are attached form a spirocyclic ring and/or R^{12} and R^{13} together with the carbon atom to which they are attached form a spirocyclic ring; or

iii. one or more of R^{10}, R^{11}, R^{12} and R^{13} form a ring together with a ring substituent of ring ***A***;

wherein, if any of substituents R^{10}, R^{11}, R^{12}, and R^{13} do not form a ring, said substituents are each independently selected from the group consisting of hydrogen; alkyl; alkenyl; haloalkyl; alkynyl; oxoalkyl; cycloalkyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; heterocyclyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; $C_{5\text{-}6}$ heteroaryl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; phenyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; hydroxyalkyl; alkoxyalkyl; aminoalkyl; *N*-alkylaminoalkyl; *N*,*N*-dialkylaminoalkyl; *N*,*N*,*N*-trialkylammoniumalkyl; thioalkyl; L^{13}–$C(O)$–$OR^{14'}$, L^{13}–$P(O)$–$(OR^{14'})_2$, or L^{13}–$S(O)_2$–$OR^{14'}$, wherein L^{13} is a bond or alkylene, and $R^{14'}$ is selected from the group consisting of hydrogen, alkyl and hydroxyalkyl; L^{15}–O–$C(O)$–$R^{16'}$, wherein L^{15} is alkylene and $R^{16'}$ is alkyl or hydroxyalkyl; L^{17}–$C(O)$–$NR^{18'}R^{19'}$, wherein L^{17} is a bond or alkylene, and $R^{18'}$ and $R^{19'}$ are each independently selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl ; and L^{20}–$NR^{21'}$–$C(O)$–$R^{22'}$, wherein L^{20} is alkylene, $R^{21'}$ is hydrogen or alkyl, and $R^{22'}$ is alkyl or hydroxyalkyl; and

as to R^{14} and R^{15},

R^{14} and R^{15} together with the carbon atom to which they are attached form a spirocyclic ring; or

one or more of R^{14} and R^{15} form a ring together with a ring atom or ring substituent of ring ***B***,

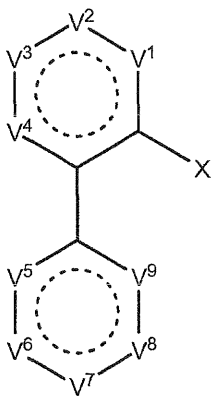
wherein, if any of substituents R^{14} and R^{15} do not form a ring, said substituents are each independently selected from the group consisting of hydrogen; alkyl; alkenyl; haloalkyl; alkynyl; oxoalkyl; cycloalkyl optionally substituted with alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl, or heteroaryl; heterocyclyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl

or haloalkoxy; C_{5-6} heteroaryl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; phenyl optionally substituted with alkyl, alkenyl, alkynyl, alkoxy, cyano, halo, haloalkyl or haloalkoxy; hydroxyalkyl; alkoxyalkyl; aminoalkyl; *N*-alkylaminoalkyl; *N*,*N*-dialkylaminoalkyl; *N*,*N*,*N*-trialkylammoniumalkyl; thioalkyl; L^{13}–C(O)–$OR^{14'}$, L^{13}–P(O)–$(OR^{14'})_2$, or L^{13}–$S(O)_2$–$OR^{14'}$ wherein L^{13} is a bond or alkylene, and $R^{14'}$ is selected from the group consisting of hydrogen, alkyl and hydroxyalkyl; L^{15}–O–C(O)–$R^{16'}$ wherein L^{15} is alkylene, and $R^{16'}$ is alkyl or hydroxyalkyl; L^{17}–C(O)–$NR^{18'}R^{19'}$, wherein L^{17} is a bond or alkylene and $R^{18'}$ and $R^{19'}$ are each independently selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl; and L^{20}–$NR^{21'}$–C(O)–$R^{22'}$, wherein L^{20} is alkylene, $R^{21'}$ is hydrogen or alkyl, and $R^{22'}$ is alkyl or hydroxyalkyl.

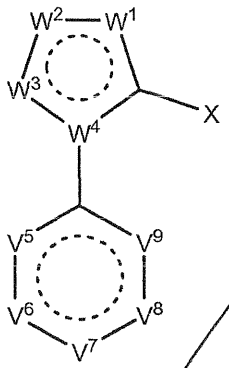
6. The process of claim **5**, wherein the ligand is selected from the group consisting of 7,7,9,9-tetramethyl-8-(2',4',6'-triisopropylbiphenyl-2-yl)-1,4-dioxa-8-phosphaspiro[4.5]decane; 2,2,6,6-tetramethyl-1-(2',4',6'-triisopropylbiphenyl-2-yl)phosphinane; 8,8,10,10-tetramethyl-9-(2',4',6'-triisopropylbiphenyl-2-yl)-1,5-dioxa-9-phosphaspiro[5.5]undecane; 2,2,6,6-tetramethyl-1-(2',4',6'-triisopropylbiphenyl-2-yl)phosphinan-4-ol; 8-(2',6'-diisopropoxybiphenyl-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane; 1,3,5,7-tetramethyl-8-(2',4',6'-triisopropylbiphenyl-2-yl)-2,4,6-trioxa-8-phosphatricyclo[3.3.1.$1^{3,7}$]decane; di-*tert*-butyl(2',4',6'-triisopropyl-3,4,5,6-tetramethylbiphenyl-2-yl)phosphine; di-*tert*-butyl(2',4',6'-triisopropylbiphenyl-2-yl)phosphine; di-*tert*-butyl(2'-isopropoxy-1,1'-binaphthyl-2-yl)phosphine; 2,2,5,5-tetramethyl-1-(2',4',6'-triisopropyl-3,4,5,6-tetramethylbiphenyl-2-yl)phospholane; 2,2,6,6-tetramethyl-1-(2',4',6'-triisopropyl-3,4,5,6-tetramethylbiphenyl-2-yl)phosphinane; 2,2,7,7-tetramethyl-1-(2',4',6'-triisopropyl-3,4,5,6-tetramethylbiphenyl-2-yl)phosphepane; 2,2,8,8-tetramethyl-1-(2',4',6'-triisopropyl-3,4,5,6-tetramethylbiphenyl-2-yl)phosphocane; 1,3,5,7-tetramethyl-8-phenyl-2,4,6-trioxa-8-phosphatricyclo[3.3.1.$1^{3,7}$]decane; 8-(2',6'-dimethoxybiphenyl-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane; 6-methoxy-*N*,*N*-dimethyl-2'-(7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decan-8-yl)biphenyl-2-amine; 8-(2'-methoxy-1,1'-binaphthyl-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane; 8-(1,1'-binaphthyl-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane; 7,7,9,9-tetramethyl-8-(2-(naphthalen-1-yl)phenyl)-1,4-dioxa-8-phosphaspiro[4.5]decane; 7,7,9,9-tetramethyl-8-(2-(naphthalen-2-yl)phenyl)-1,4-dioxa-8-phosphaspiro[4.5]decane; 2,2,6,6-tetramethyl-1-(2',4',6'-triisopropylbiphenyl-2-yl)phosphinan-4-one; 3,3,8,8,10,10-hexamethyl-9-(2',4',6'-triisopropylbiphenyl-2-yl)-1,5-dioxa-9-phosphaspiro[5.5]undecane; 1-(2'-(dimethylamino)-6'-methoxybiphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(2',6'-bis(dimethylamino)biphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(2',6'-dimethoxybiphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(2',6'-diisopropoxybiphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(2'-(dimethylamino)biphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(biphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(1,1'-binaphthyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(2'-methoxy-1,1'-binaphthyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one;

1-(3,6-dimethoxybiphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(3,6-dimethoxy-2',4',6'-trimethylbiphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 2,2,6,6-tetramethyl-1-(2',4',6'-triisopropyl-3,6-dimethoxybiphenyl-2-yl)phosphinan-4-one; 2,2,6,6-tetramethyl-1-(2',4',6'-triisopropyl-4,5-dimethoxybiphenyl-2-yl)phosphinan-4-one; 1-(3',5'-dimethoxybiphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; 1-(4'-*tert*-butylbiphenyl-2-yl)-2,2,6,6-tetramethylphosphinan-4-one; N^2,N^2,N^6,N^6-tetramethyl-2'-(7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decan-8-yl)biphenyl-2,6-diamine;*N*,*N*-dimethyl-2'-(7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decan-8-yl)biphenyl-2-amine; 8-(biphenyl-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane; 8-(3,6-dimethoxybiphenyl-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane; and 8-(3,6-dimethoxy-2',4',6'-trimethylbiphenyl-2-yl)-7,7,9,9-tetramethyl-1,4-dioxa-8-phosphaspiro[4.5]decane.

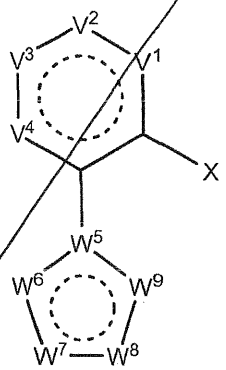
7. The process of claim **5**, wherein said phosphine ligand has a structure corresponding to a structure of a formula selected from the group consisting of formulae (I-1) - (I-42),



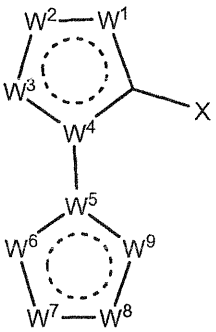
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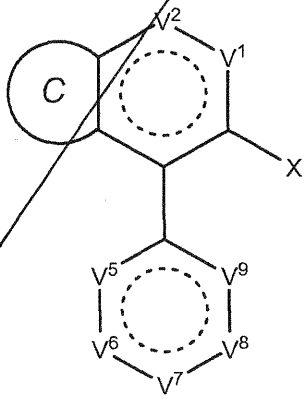
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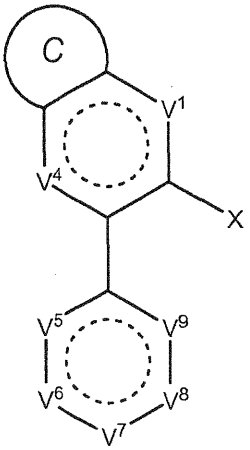
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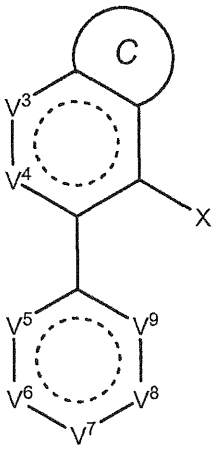
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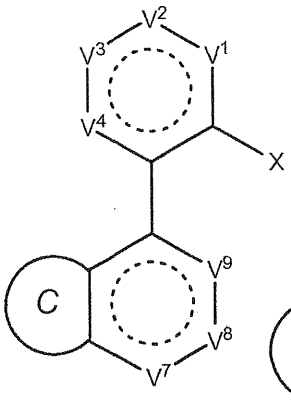
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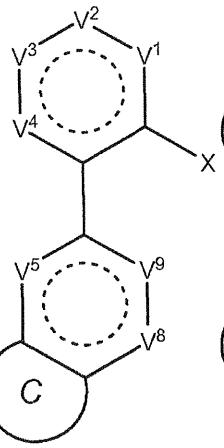
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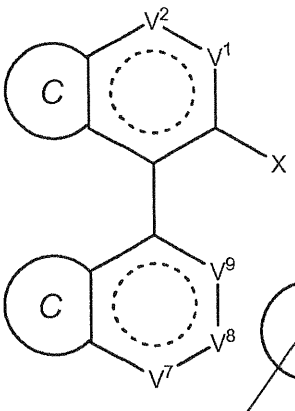
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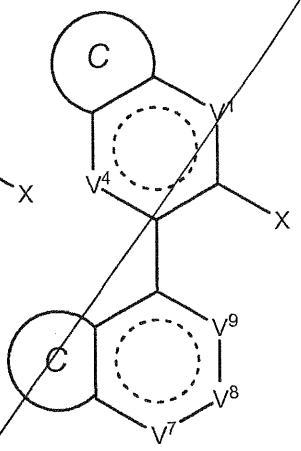
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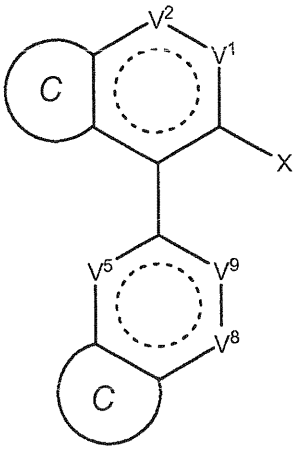
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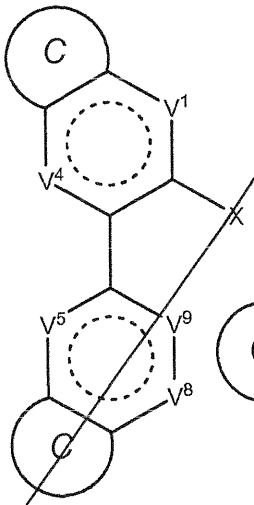
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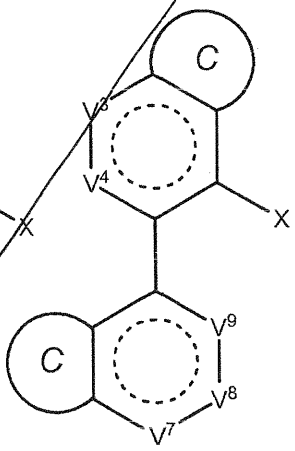
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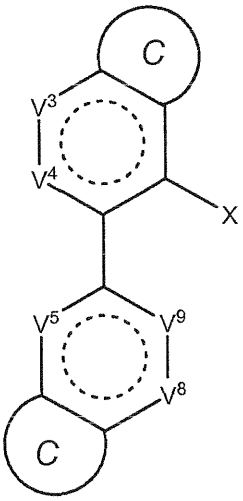
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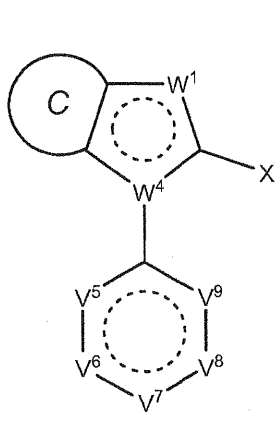
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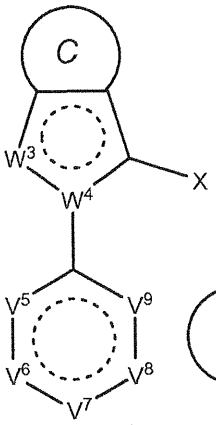
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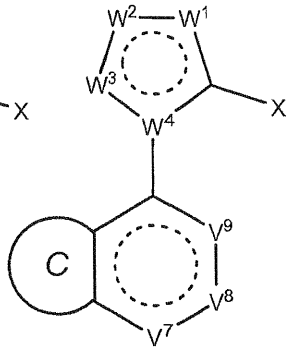
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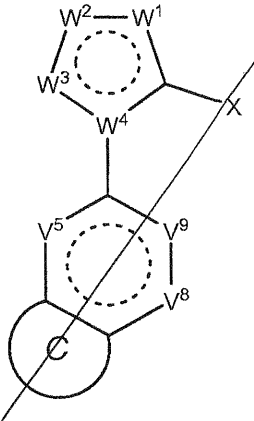
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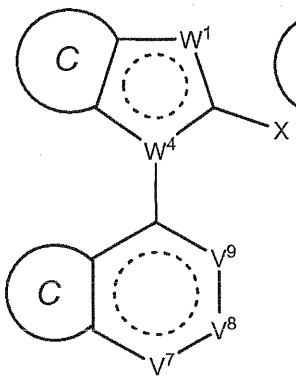
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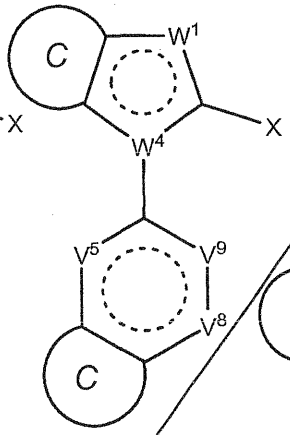
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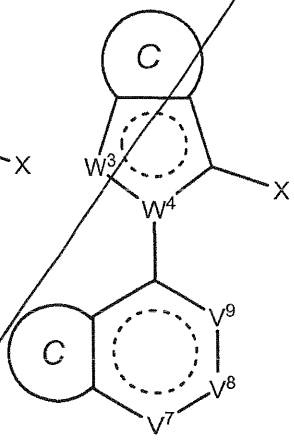
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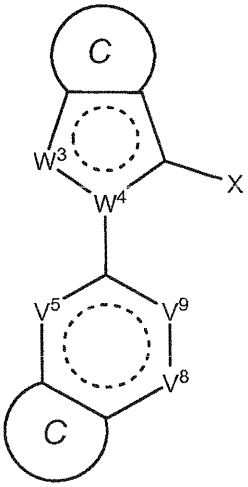
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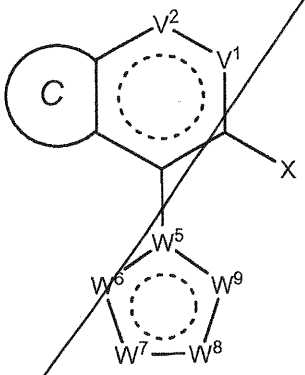
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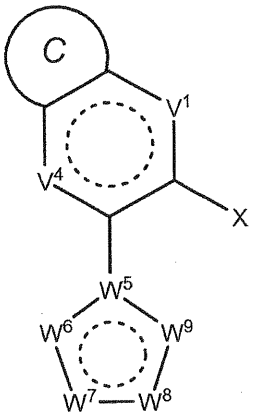
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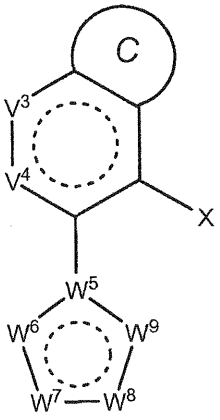
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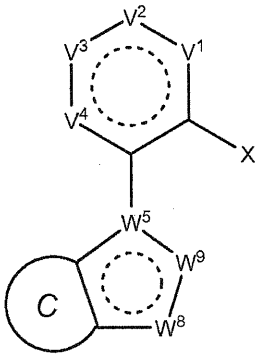
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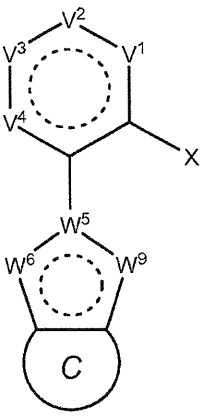
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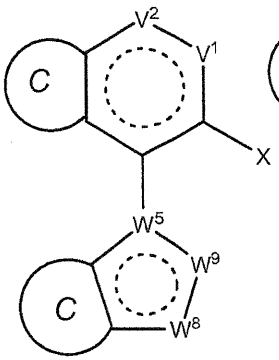
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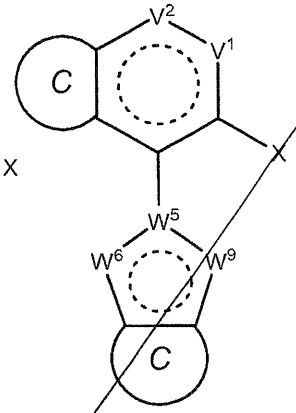
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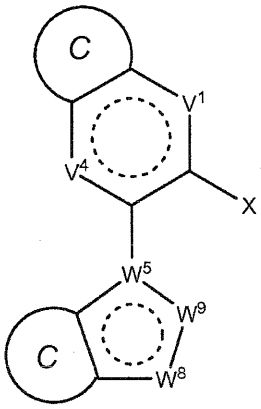
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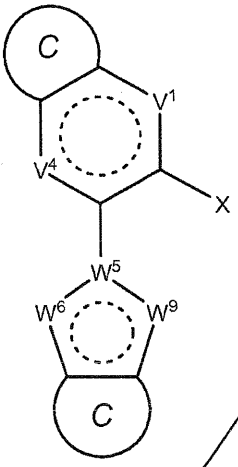
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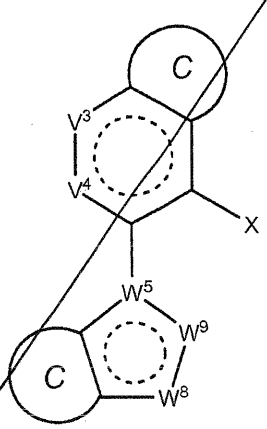
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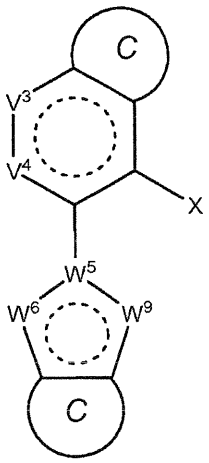
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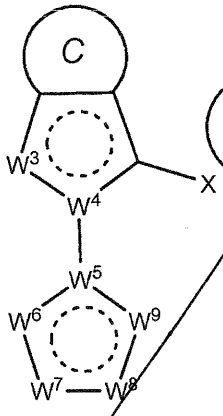
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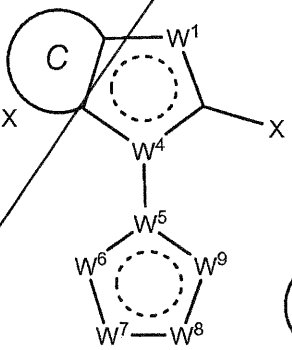
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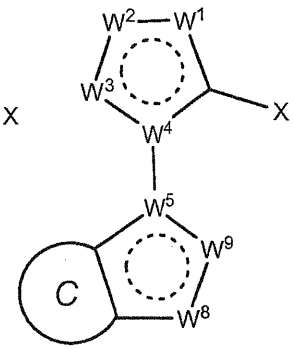
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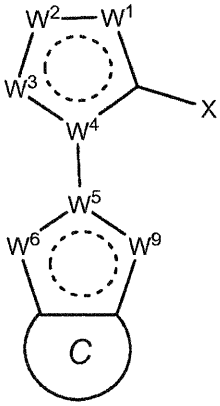
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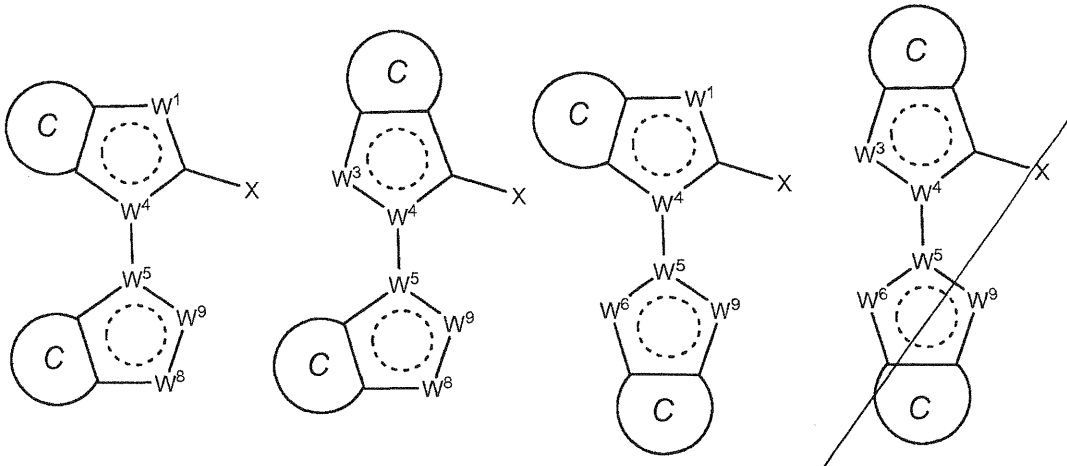
(I-36)



(I-37)



(I-38)



(I-39) (I-40) (I-41) (I-42)

or a salt thereof, wherein

X is a phosphine of formula (Ia) or (Ib);

V^1, V^2, V^3, and V^4 are each independently CR^1 or N;

V^5, V^6, V^7, V^8 and V^9 are each independently CR^2 or N;

W^1, W^2, an W^3 are each independently selected from the group consisting of CR^1, NR^1, N and O;

W^4 is C or N;

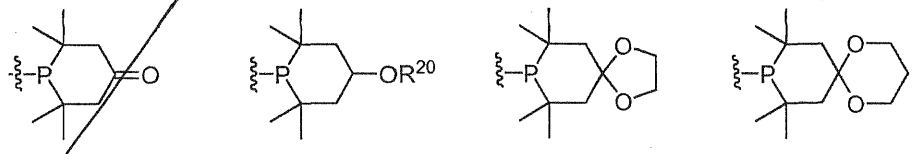
W^5 is C or N;

W^6, W^7, W^8 and W^9 are each independently selected from the group consisting of CR^2, NR^2, N and O;

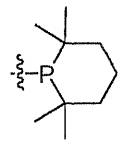
and

ring ***C***, at each occurrence, is a fused-aryl or fused-heteroaryl and is optionally substituted with R^1 and R^2.

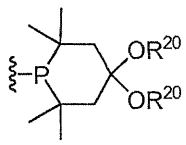
8. The process of claim **5**, wherein X is a phosphine having a structure corresponding to a formula selected from the group consisting of:



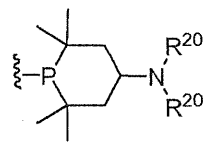
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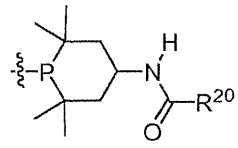
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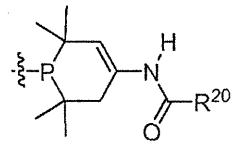
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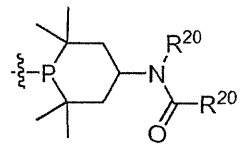
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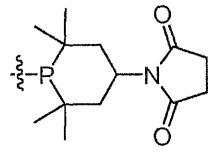
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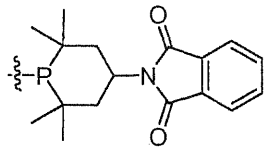
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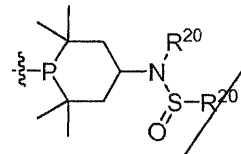
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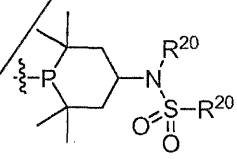
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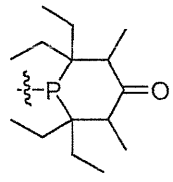
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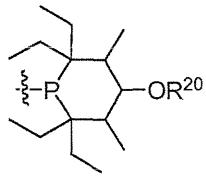
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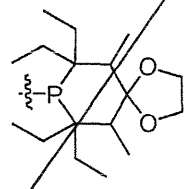
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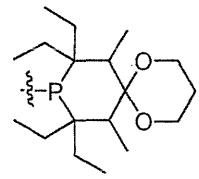
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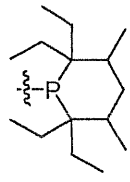
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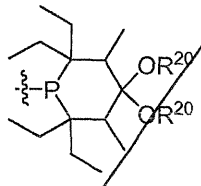
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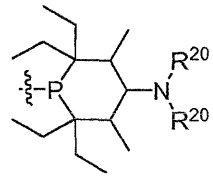
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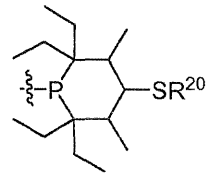
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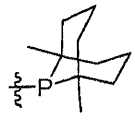
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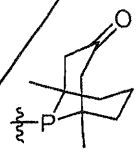
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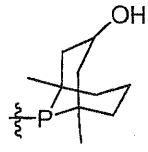
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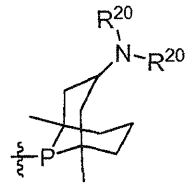
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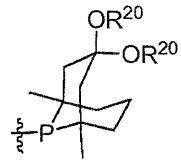
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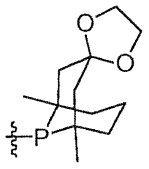
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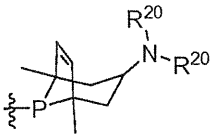
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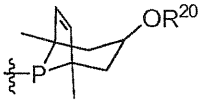
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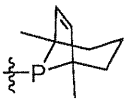
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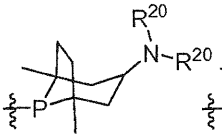
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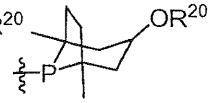
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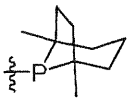
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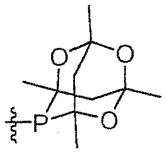
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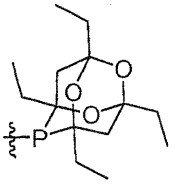
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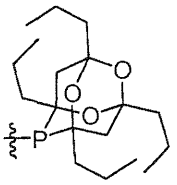
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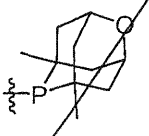
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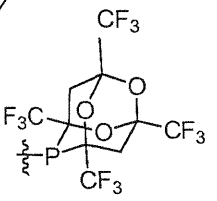
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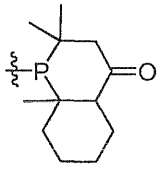
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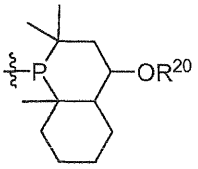
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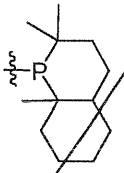
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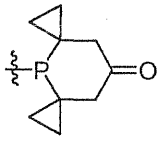
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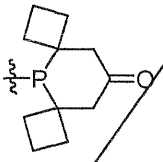
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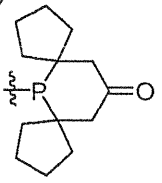
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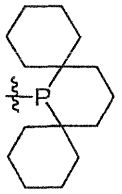
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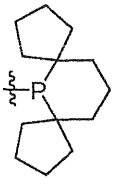
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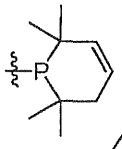
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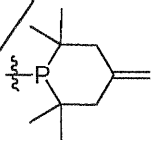
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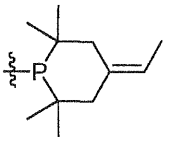
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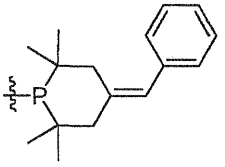
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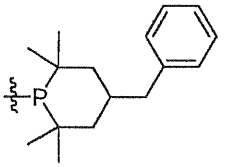
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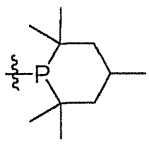
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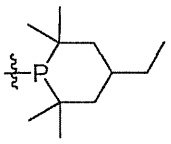
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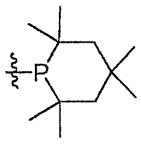
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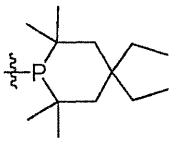
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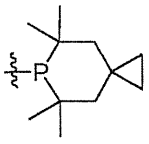
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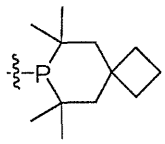
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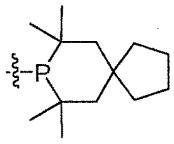
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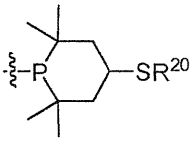
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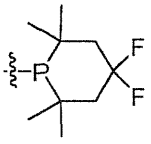
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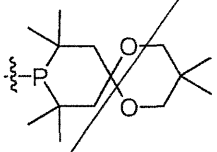
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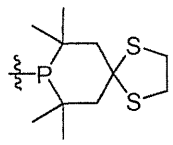
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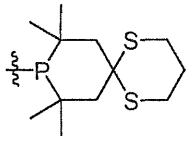
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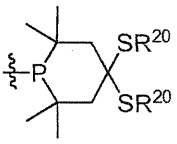
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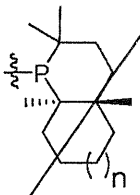
1-65



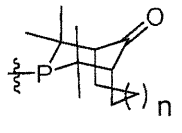
1-66



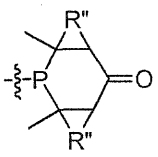
1-67



1-68



1-69, and



,

1-70

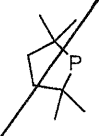
or a salt thereof, wherein

R" is selected from the group consisting of oxygen, NR^{20}, and $C(R^{20})_2$;

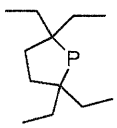
R^{20} is hydrogen or alkyl; and

n is 0, 1, or 2.

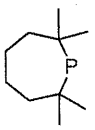
9. The process of claim **5**, wherein X is a phosphine having a structure corresponding to a formula selected from the group consisting of



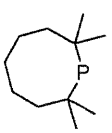
2-1



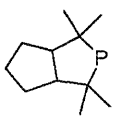
2-2



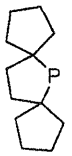
2-3



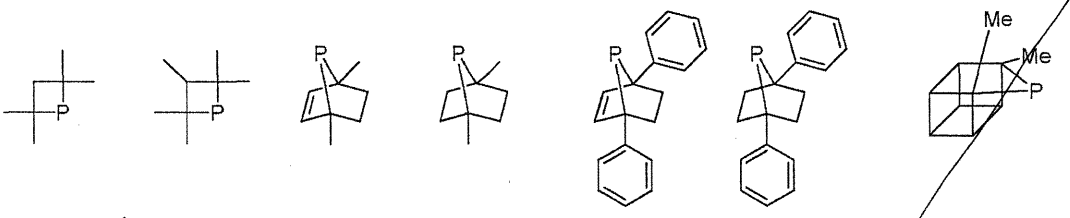
2-4



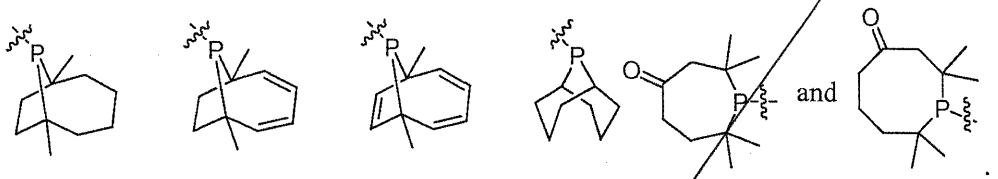
2-5



2-6



2-7 2-8 2-9 2-10 2-11 2-12 2-13



2-14 2-15 2-16 2-17 2-18 2-19

10. The process of claim **3**, wherein the transition metal catalyst precursor is a palladium catalyst precursor.

11. The process of claim **10**, wherein the palladium catalyst precursor is selected from the group consisting of tetrakis(triphenylphosphine)palladium(0), dichlorobis(tri-*o*-tolylphosphine)palladium(II), palladium(II) acetate, [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), tris(dibenzylideneacetone)dipalladium(0), dichloro(dibenzylideneacetone)dipalladium(II), dichlorotris(cyclohexylphosphine) palladium(II), dichlorobis(triphenyl-phosphine) palladium(II), chloro(η3-allyl)palladium(II) dimer-triphenylphosphine, palladium(II) chloride, palladium(II) bromide, and bis(acetonitrile)dichloropalladium(II).

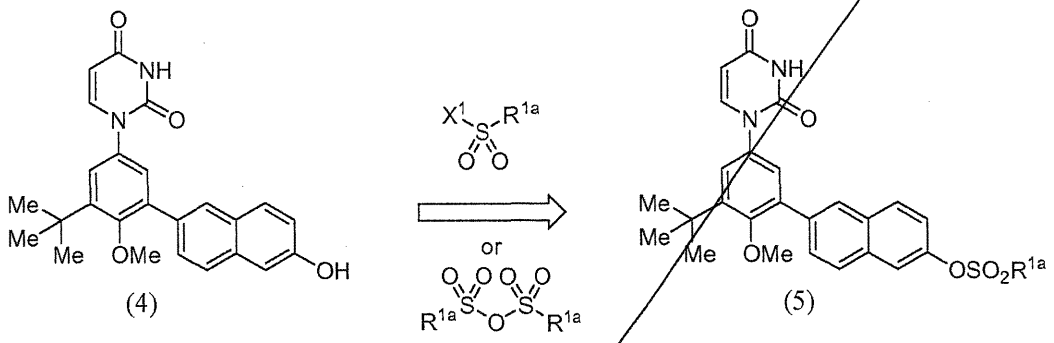
12. The process of any one of claims **1-11**, wherein compound **(5)** is sulfonamidated in the presence of a base.

13. The process of claim **12**, wherein the base is selected from the group consisting of potassium phosphate tribasic, cesium carbonate, potassium carbonate, sodium carbonate, sodium *tert*-butoxide, potassium *tert*-butoxide, lithium bis(trimethylsilyl)amide, and lithium diisopropylamide.

14. The process of any one of claims **1-13**, wherein compound **(5)** is sulfonamidated in the presence of solvent.

15. The process of claim **14**, wherein the solvent is selected from the group consisting of tetrahydrofuran, *N*,*N*-dimethylformamide, *N*,*N*-dimethylacetamide, *N*-methyl- pyrrolidone, dimethyl sulfoxide, 1,2-dimethoxyethane, 1,4-dioxane, acetonitrile, cyclopentyl methyl ether, toluene, benzene, *tert*-amyl alcohol, and *tert*-butyl alcohol.

16. The process of any one of claims **1-15**, wherein compound **(5)** is prepared by sulfonylating 1-(3-*tert*-butyl-5-(6-hydroxynaphthalen-2-yl)-4-methoxyphenyl)pyrimidine-2,4(1*H*,3*H*)-dione (compound **4**).



wherein

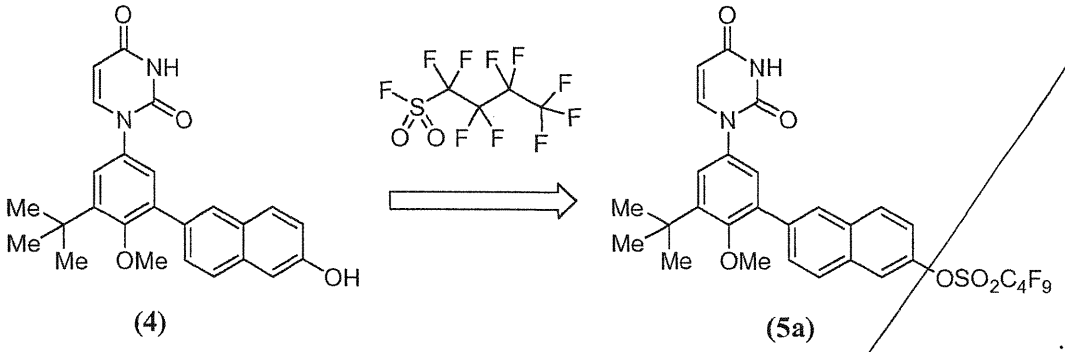
X^1 is selected from the group consisting of chlorine and fluorine; and

R^{1a} is selected from the group consisting of *p*-tolyl, phenyl, methyl, ethyl, trifluoromethyl, perfluorobutyl, perfluoropentyl, perfluorohexyl, perfluorooctyl, and isomers and homologs thereof

17. The process of claim **16**, wherein the sulfonyl compound is perfluorobutanesulfonyl fluoride.

18. The process of any one of claims **1-17**, wherein R^{1a} is perfluorobutyl.

19. The process of claim **18**, wherein compound **(5)** is prepared by reacting 1-(3-*tert*-butyl-5-(6-hydroxynaphthalen-2-yl)-4-methoxyphenyl)pyrimidine-2,4(1*H*,3*H*)-dione (compound **4**) with perfluorobutanesulfonyl fluoride:

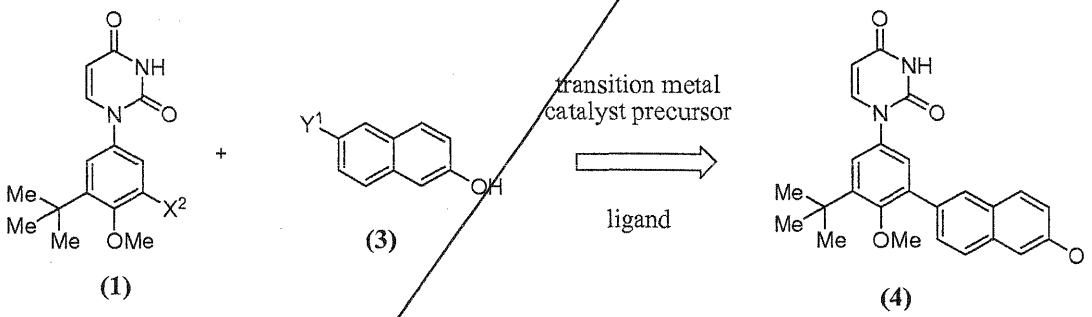


(4) (5a)

20. The process of claim **19**, wherein compound (**4**) and perfluorobutanesulfonyl fluoride are reacted in the presence of base.

21. The process of any one of claims **19** and **20**, wherein compound (**4**) and perfluorobutanesulfonyl fluoride are reacted in the presence of solvent.

22. The process of any one of claims **19-21**, wherein compound (**4**) is prepared by a process comprising coupling compound (**1**) with compound (**3**):



(1) (3) (4)

wherein

X^2 of compound (**1**) is selected from the group consisting of chlorine, bromine and iodine; and

Y^1 of compound (**3**) is selected from the group consisting of boronic acid, borate ester, and borate salt.

23. The process of claim **22**, wherein compound (**1**) is 1-(3-*tert*-butyl-5-iodo-4-methoxyphenyl)pyrimidine-2,4(1*H*,3*H*)-dione (compound (**1c**)).

24. The process of claim **22**, wherein compound (**3**) is 6-hydroxynaphthalen-2-ylboronic acid (compound (**3a**)).

25. The process of claim **22**, wherein compound **(1)** and **(3)** are coupled using a transition metal catalyst precursor and ligand.

26. The process of claim **25**, wherein the ligand is a phosphine.

27. The process of claim **25**, wherein the phosphine ligand is selected from the group consisting of tri-*t*-butylphosphine, tricylcohexylphosphine, tris(2-furyl)phosphine, 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, 1,3,5,7-tetramethyl-8-phenyl-2,4,6-trioxa-8-phosphatricyclo[3.3.1.$1^{3,7}$]decane, biphenyl-2-yldicyclohexylphosphine, dicyclohexyl(2',6'-dimethoxybiphenyl-2-yl)phosphine, and dicyclohexyl(2',4',6'-triisopropylbiphenyl-2-yl)phosphine.

28. The process claim **25**, wherein the transition metal catalyst precursor is a palladium catalyst precursor.

29. The process of claim **28**, wherein the palladium catalyst precursor is selected from the group consisting of tetrakis(triphenylphosphine)palladium(0), dichlorobis(triphenylphosphine)palladium(II), tris(dibenzylidineacetone)dipalladium, palladium(II) diacetate, dichlorobis(triphenylphosphine)palladium, and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane.

30. The process of any one of claims **22-28**, wherein compounds **(1)** and **(3)** are coupled in the presence of a base.

31. The process of claim **30**, wherein the base is selected from the group consisting of potassium phosphate tribasic, cesium carbonate, potassium carbonate, sodium carbonate, potassium *tert*-butoxide and cesium fluoride.

32. The process of any one of claims **22-31**, wherein compounds **(1)** and **(3)** are coupled in the presence of a solvent.

33. The process of claim **32**, wherein the solvent is selected from the group consisting of tetrahydrofuran, *N*,*N*-dimethylformamide, 1,2-dimethoxyethane, 1,4-dioxane, ethanol, toluene, water and mixtures thereof.

34. The process of claim **1**, wherein compound **(A)** is converted to a corresponding salt, compound **(As)**.

35. The process of claim **34**, wherein compound **(A)** is converted to compound (**As**) by treatment with a base.

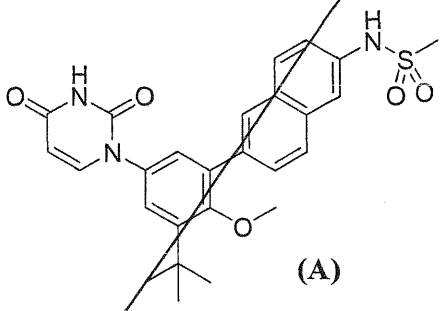
36. The process of claim **35**, wherein the base is sodium hydroxide or potassium hydroxide.

37. The process of claim **34**, wherein compound **(A)** is converted to compound (**As**) in the presence of a solvent.

38. The process of claim **37**, wherein the solvent is selected from the group consisting of dimethyl sulfoxide, 2-propanol, water and mixtures thereof.

39. The process of claim **34**, wherein compound (**As**) is a sodium salt.

40. A compound or salt thereof prepared by the process of any one of claims **1-15**, wherein the compound corresponds in structure to the following formula:



(A)

41. The salt according to claim **40**, wherein the salt is sodium.

42. A pharmaceutical composition comprising the compound of claim **40**, and a pharmaceutically acceptable carrier.

43. The pharmaceutical composition of claim **42**, which further comprises one, two, three, four, five or six agents selected from the group consisting of a second HCV polymerase inhibitor, an HCV protease inhibitor, interferon, ribavirin, and an anti-HIV agent.

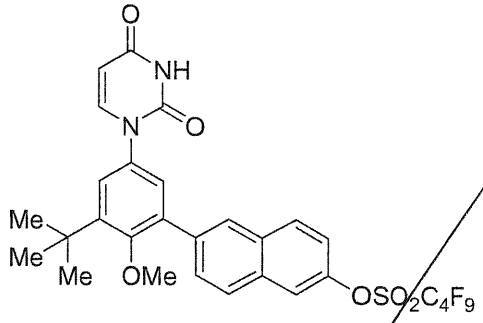
44. Use of the compound of claim **41**, in the manufacture of a medicament for treating a disease treatable by inhibiting HCV RNA polymerase.

45.

Use of the compound of claim **41**, in the manufacture of a medicament for inhibiting the replication of an HCV virus .

46. Use of compound of claim **41**, in the manufacture of a medicament for treating or preventing an HCV infection.

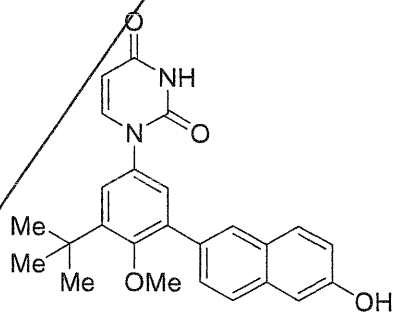
47. A compound or salt thereof, wherein the compound corresponds in structure to formula **(5a)**:



(5a)

48. The compound of claim **47**, wherein the compound is prepared by the process of any one of claims **19-21**.

49. A compound or salt thereof prepared by the process of any one of claims **22-33**, wherein the compound corresponds in structure to the following formula:



(4)