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Chelating Retardation Effect in Nickel Assisted Phosphination: Syntheses of Atropisomeric *P,N* Ligands

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Abstract—$Ni(PPh_3)_2Cl_2$ was found to be an effective reagent in nickel assisted phosphination of biaryl *O,N* triflates with chlorodiphenylphosphine to yield atropisomeric *P,N* ligands. The chelating effect of the substrates in the reaction played an important role. Only the monodentate PPh_3 rather than bidentate dppe (1,2-bis(diphenylphosphino)ethane) nickel complex was found to be an effective reagent.

Introduction

Atropisomeric phosphine ligands have played a crucial role in the development of asymmetric catalysis. The most successful phosphine is the well known 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP)[1] **4** ligand which was firstly reported in 1980 and applied to many asymmetric catalysis.[2] This discovery of the BINAP ligand initiated the development of other mixed donor atropisomeric ligands based on the binaphthyl or other biaryl backbones such as QUINAP[3] **5** and MAP **6**[4] (Fig. 1).

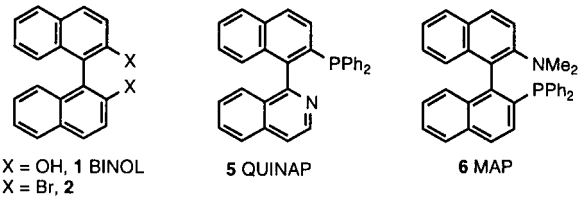
This class of hemilabile ligands possesses a combination of hard and soft donor atoms, and have different features associated with each donor atom that provide unique reactivity to their metal complexes.[5] One important property of these potential ligands is that they can stabilize metal ions in a variety of oxidation states and geometries. Moreover, the hard ends weakly coordinate to soft metal centers and easily dissociate in solution to afford a vacant site whenever demanded. On the other hand, their chelating effect confers stability to the catalyst in the absence of substrates. In addition, *P,N* ligands can display quite different coordination modes compared with *P,P* and *N,N* ligands.[6,7] The π-acceptor character of the phosphorus ligand can stabilize a metal center in a low oxidation state, while the nitrogen σ-donor ability makes the metal more susceptible to oxidative addition reactions. Recently, the attention has been focused on *P,N* ligands that they have been used very successfully in asymmetric catalytic reactions such as allylic substitution,[8] hydrosilylation,[9] hydroboration–oxdation,[10] hydroboration–amination,[11] and transfer hydrogenation reactions.[12] Herein, we report the synthesis of new atropisomeric *P,N* ligands by nickel assisted phosphination and the chelation effect in the reaction cycle.

Results and Discussion

Initial attempts to convert the aromatic hydroxyl group of pyridylphenol **8a** to pyridylphenyl bromide **7** by the reaction with triphenylphosphine dibromide did not yield any bromide **7**. The starting material **8a** decomposed likely due to the extreme high reaction temperature (320°C).[13]

Alternatively, pyridylphenol **8a** was transformed into the corresponding pyridylphenyl triflate **8b** by using trifluoromethanesulfonic anhydride (triflic anhydride) in the presence of excess 4-(*N,N*-dimethyl)aminopyridine[14] (DMAP) or pyridine[15,16] in dry dichloromethane in 95% yield (Scheme 1). Similarly, biaryl pyridylphenols[17,3a] **8a**–**12a** were also transformed into the corresponding *O,N* triflates **8b**–**12b** respectively in good yield (Scheme 1).

In the nickel catalyzed phosphination of aryl triflates, Hiemstra and co-workers reported the failed transformation



X = OH, **1** BINOL
X = Br, **2**
X = OTf. **3**
X = PPh_2, **4** BINAP

5 QUINAP

6 MAP

Figure 1. Atropisomeric ligands.

Keywords: bis(triphenylphosphine) nickel(II) dichloride; *P,N* ligand; phosphination.
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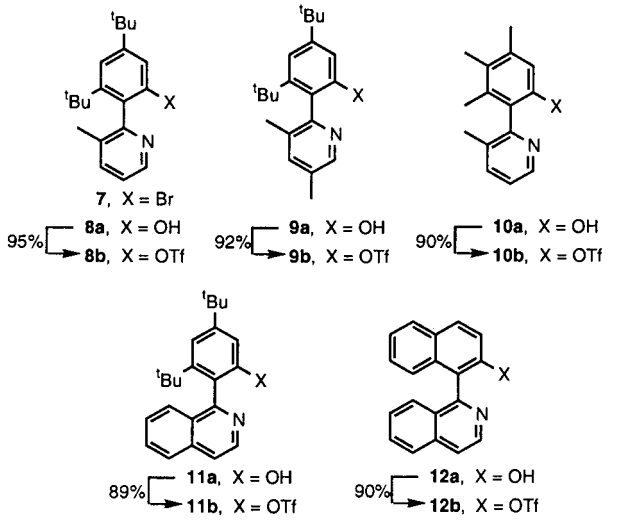


Scheme 1. Trifluoromethanesulfonation of quinolyl and pyridylphenols. (conditions: 1.1 equiv. Tf_2O, 3 equiv. pyridine, dry CH_2Cl_2, room temperature)

of BIFOL ditriflates **13** into BIFAP **14** even with prolonged reaction time at elevated temperature and the use of stoichiometric amount of Ni(dppe)Cl_2 catalyst (Fig. 2).[18] However, the sterically less hindered benzofuranyl triflate **15** was reactive enough and gave the monophosphine product **16** in moderate yield (Fig. 2).[18] Therefore, the steric hindrance in nickel catalyzed phosphination imposes the limitation on the size of *ortho*-substitutent in aryl triflate substates.[19]

Apart from the steric hindrance, we found that the chelating substrate inhibited the nickel assisted phosphination. Attempted phosphination of pyridylphenyl triflate **8b** by using nickel catalyzed phosphination with diphenylphosphine[20] or chlorodiphenylphosphine[21] did not yield any of the desired *P*,*N*product **8c** (Scheme 2).[22,23]

The problem of failed phosphination of this substrate may be due to the steric or chelation inhibition. In order to investigate the possibility of chelation inhibition, a control experiment with coordinating additive was designed for the phosphination of BINOL ditriflates **3** to BINAP **4**. The addition of two equivalents of pyridine to the nickel catalyzed phosphination of BINOL ditriflates **3** showed that only a trace amount of BINAP was detected even with extended reaction time with most of the starting material recovered (Table 1, entries 1 and 2). In the absence of pyridine, same as with literature report, BINAP was obtained in moderate yield.[21] The failed conversion of BINOL ditriflates **3** to BINAP **4** in the presence of added pyridine suggested that the unsuccessful synthesis of *P*,*N*

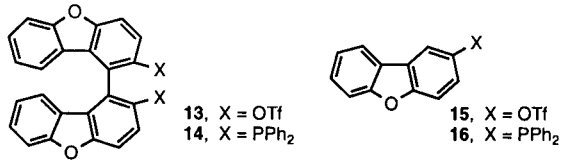
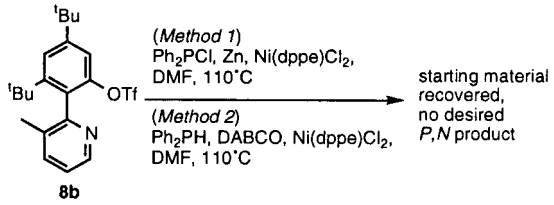


Figure 2. Steric effect in phosphination of BIFOL ditriflate.



Scheme 2. Literature methods in phosphination.[20,21]

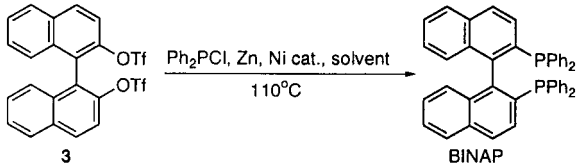
ligand was probably due to the coordinating pyridyl group of the substrate apart from possible steric hindrance. The inactivity of the nickel catalyst may be due to the hard pyridyl group, which chelates the hard nickel center and renders the complex coordinatively saturated.[24] A similar chelating inhibition effect was also observed in the Rh catalyzed hydrogenation with pyridylphosphines.[25]

When the catalyst was changed from the bidentate Ni(dppe)Cl_2 into monodentate Ni(PPh_3)$_2Cl_2$, the corresponding BINAP was obtained even in the presence of added pyridine in the phosphination of BINOL ditriflate **3** (Table 1, entries 3 and 4). Presumably, the monodentate triphenylphosphine dissociated more easily in the course of the reaction and provided a vacant coordination site for the nickel center. The monodenate Ni(PPh_3)$_2Cl_2$ was then applied to the *O*,*N* triflate **8b** for the successful synthesis of *P*,*N* ligand **8c** (Table 2, entry 1 and 2).

In order to optimize the reaction conditions, other polar aprotic solvents were screened. *N*,*N*-Dimethylpyrolidinone (NMP) was found to be suitable for this reaction but the ratio of phosphine to reduction product was lower than in DMF solvent (Table 2, entries 2 and 3). However, the less polar solvent THF proved to be inferior (Table 2, entry 4). When the reaction temperature was lowered, a higher ratio of phosphine to reduction product was obtained but longer reaction time was required and an extremely low yield of **8c** was obtained (Table 2, entry 5). Moreover, the monodentate Ni(PPh_3)$_2Br_2$ complex was also found to be effective for the phosphination (Table 2, entry 6).

The optimized Ni(PPh_3)$_2Cl_2$ assisted phosphination was found to be applicable for the synthesis of other atropisomeric *P*,*N* ligands **8c**–**11c** and QUINAP[3a] **12c** from their corresponding *O*,*N* triflates (Table 3). The relatively

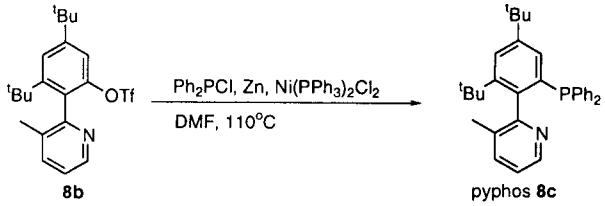
Table 1. Pyridine inhibitory effect in nickel assisted phosphination



Entry	Catalysts	Solvent	Time/d	Yield[a] (%)
1	Ni(dppe)Cl_2	DMF	1.5	35
2	Ni(dppe)Cl_2	DMF, 2eq. Py	3	Trace[b]
3	Ni(PPh_3)$_2Cl_2$	DMF	1.5	30
4	Ni(PPh_3)$_2Cl_2$	DMF, 2eq. py	2	29

[a] Isolated yield.
[b] Starting material was recovered.

Table 2. Nickel assisted phosphination of *O,N* triflates with chlorodiphenylphosphine



8b pyphos 8c

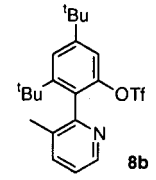
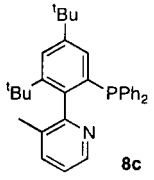
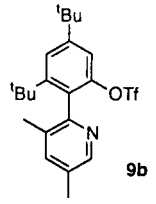
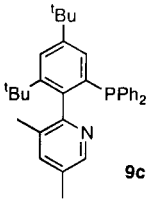
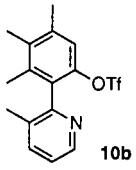
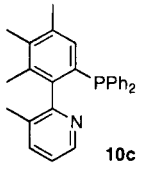
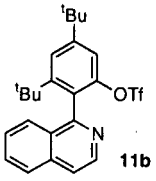
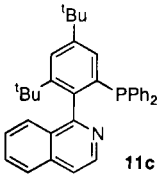
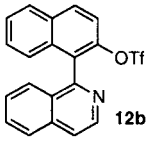
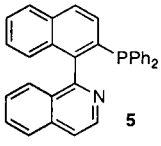
Entry	Catalyst	Solvent	Temp (°C)	Time/d	H:PPh_2 ratio[a]	Yield (%)[b]
1	$Ni(dppe)Cl_2$	DMF	110	5	/	0
2	$Ni(PPh_3)_2Cl_2$	DMF	110	1.5	2:3	41
3	$Ni(PPh_3)_2Cl_2$	NMP	110	4	3:2	15
4	$Ni(PPh_3)_2Cl_2$	THF	110	5	/	0
5	$Ni(PPh_3)_2Cl_2$	DMF	50	11	1:7	2
6	$Ni(PPh_3)_2Br_2$	DMF	110	1.5	2:3	20

[a] Estimated by ^1H NMR integration.
[b] Isolated yield of phosphine product.

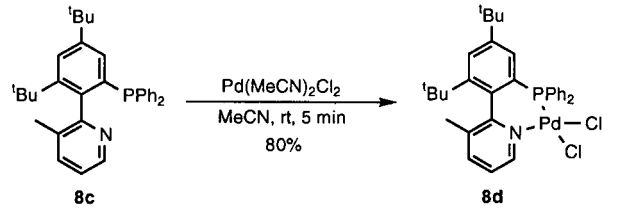
stronger pyridine coordinating substrates required longer reaction time (Table 3, entry 1–3). The less coordinating isoquinolyl substrates reacted a little faster (Table 3, entry 4 and 5). Presumably the stronger coordinating group showed a stronger chelating retardation effect in the nickel assisted phosphination.

The synthesized atropisomeric *P,N* ligand pyphos was

Table 3. Syntheses of atropisomeric *P,N* ligands

Entry	Substrates	Products	Time/d	H:PPh_2 ratio[a]	Yield/ %[b]
1	 **8b**	 **8c**	1.5	2:3	41
2	 **9b**	 **9c**	2.0	1:1	40
3	 **10b**	 **10c**	1.5	1:1	38
4	 **11b**	 **11c**	1.0	1:2	41
5	 **12b**	 **5**	1.0	1:2	42

[a] Estimated by ^1H NMR integration.
[b] Isolated yield of phosphine products.



Scheme 3. Metallation of pyphos.

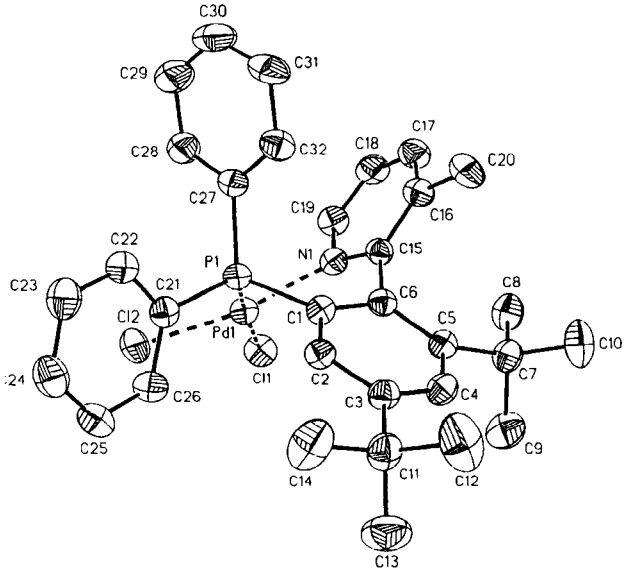


Figure 3. X-Ray crystal structure of Pd–pyphos complex.

metallated with bis-acetonitrilepalladium(II) dichloride in acetonitrile at room temperature to form the Pd–pyphos complex **8d** in 80% yield (Scheme 3). The crystal structure of Pd–pyphos showed that both the phosphine group and pyridine group coordinate to the palladium center (Fig. 3). Therefore pyphos behaves as a bidentate ligand. The biaryl *P,N* ligand possesses a dihedral angle of 73° between the phenyl and pyridyl rings.

Conclusion

In conclusion, the chelation inhibition of nickel assisted phosphination with Ph_2PCl was observed. Modified conditions using $Ni(PPh_3)_2Cl_2/Zn/Ph_2PCl$ were found for the successful preparation of *P,N* ligands from pyridylphenols via pyridylphenyl triflates.

Experimental

Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. THF was distilled from sodium benzophenone ketyl immediately prior to use. DMF and NMP were distilled from magnesium sulfate under nitrogen.[26] Zinc was activated by washing with dilute hydrochloric acid followed by water, ethanol and dry ether.[26] $Ni(PPh_3)_2Cl_2$ and $Ni(PPh_3)_2Br_2$ were prepared from $NiCl_2$ and $NiBr_2$ hydrate respectively according to the literature method.[27] Thin layer chromatography was performed on silica gel 60 F_{254} plates. Silica gel (70–230 and 230–400 mesh) was used for column chromatography.

^1H NMR spectra were recorded at 300 MHz and the chemical shifts were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm), or with tetramethylsilane (TMS) (δ 0.00 ppm) as the internal standard. ^{13}C NMR spectra were obtained at 75 MHz and referenced to the residual $CHCl_3$ (δ 77.0 ppm) in $CDCl_3$. ^{31}P NMR spectra were obtained at 162 MHz and chemical shifts were referenced to 85% H_3PO_4 (δ 0.00 ppm) externally. Mass spectra were recorded either in electron ionization (EI) or fast atom bombardment (FAB) mode using *m*-nitrobenzyl alcohol (NBA) as the matrix. X-Ray data has been deposited in Cambridge Crystallographic Center.

General procedure for trifluoromethanesulfonation of pyridylphenols

3,5-Di-*tert*-butyl-2-(3′-methyl-2′-pyridyl)phenyl trifluoromethanesulfonate (8b). 3,5-Di-*tert*-butyl-2-(3′-methyl-2′-pyridyl)phenol[17] (**8a**) (297 mg, 1.0 mmol) was dissolved in dry dichloromethane (5 mL) under nitrogen at room temperature in a three-necked round bottom flask. Pyridine (0.26 mL, 3.0 mmol) was added under nitrogen. Trifluoromethanesulfonic anhydride (triflic anhydride) (0.18 mL, 1.1 mmol) in dry dichloromethane (3 mL) was then added dropwise to the reaction mixture. White fumes evolved and the color of the solution changed from yellow to orange. The reaction mixture was stirred at room temperature for 2 h. Water (5 mL) was added and the aqueous phase was extracted by dichloromethane (20 mL×3). The combined organic extract was washed with water, brine, and dried over $MgSO_4$. The solvent was removed by rotary-evaporation to give the brown residue which was purified by column chromatography on silica gel using a solvent mixture (hexane/ethyl acetate =5:1) as the eluent to afford 3,5-di-*tert*-butyl-2-(3′-methyl-2′-pyridyl)phenyl trifluoromethanesulfonate (**8b**) (408 mg, 95%) as a white solid. R_f=0.6 (hexane/ethyl acetate=4:1); mp 96–98°C; ^1H NMR (300 MHz, $CDCl_3$) δ 1.16 (s, 9H), 1.36 (s, 9H), 2.12 (s, 3H), 7.20 (s, 1H), 7.23 (dd, 1H, J=7.8 Hz, 4.8 Hz), 7.57 (d, 1H, J=8.0 Hz), 7.63 (d, 1H, J=0.8 Hz), 8.53 (d, 1H, J=4.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 29.7, 31.1, 35.1, 37.5, 115.4, 118.2 (q, J_{CF}=317.6 Hz), 124.4, 132.7, 133.1, 138.3, 146.4, 148.2, 150.5, 152.1, 152.5; MS (EI): *m/z* (relative intensity) 430 (M^++1, 74), 414 (52), 296 (19), 281 (100), 266 (22); HRMS (ESIMS) calcd for $C_{21}H_{26}F_3NO_3SH^+$ 430.1658, found 430.1647.

General procedure for nickel assisted phosphination of *O,N* triflates

2-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (pyphos) (8c). To a solution of 3,5-di-*tert*-butyl-2-(3′-methyl-2′-pyridyl)phenyl trifluoromethanesulfonate (**8b**) (107 mg, 0.25 mmol) and bis(triphenylphosphine) nickel(II) chloride (82 mg, 0.13 mmol) in dry DMF (1 mL) under nitrogen in a Teflon stopcock flask. Chlorodiphenylphosphine (45 μL, 0.25 mmol) was added counterflow with nitrogen and Zn (11 mg×3, 0.5 mmol) was then added in three portions. The color of the solution

was gradually changed from blue to dark red. The solution was heated to 110°C under nitrogen for 1.5 days. The reaction mixture was then cooled down and the solvent was removed by vacuum evaporation. The residue was redissolved in dichloromethane and purified by short column chromatography on silica gel using a solvent mixture of (hexane/ethyl acetate=6:1, R_f=0.6) as eluent to obtain the crude product. This crude product was then purified by column chromatography on silica gel with eluent (toluene/ethyl acetate=20:1) to afford the 2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (pyphos) (**8b**) (47 mg, 41%) as a light yellow solid. R_f=0.6 (toluene/ethyl acetate=15:1); mp 135–137°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.13 (s, 9H), 1.17 (s, 9H), 1.94 (s, 3H), 7.04–7.30 (m, 13H), 7.60 (d, 1H, J=2.0 Hz), 8.34 (d, 1H, J=4.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.9, 31.1, 32.4, 34.8, 37.2, 125.8, 127.9, 128 (d, J_{CP}=8.0 Hz), 128.2 (d, J_{CP}=4.6 Hz), 130.1, 131.2 (d, J_{CP}=7.6 Hz), 131.1 (d, J_{CP}=7.5 Hz), 133.4 (d, J_{CP}=19.3 Hz), 134.0 (d, J_{CP}=20.0 Hz), 137.1 (d, J_{CP}=8.7), 138.0 (d, J_{CP}=9.3 Hz), 138.2, 145.1, 147.1 (d, J_{CP}=5.6 Hz), 149.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.60; MS (EI): *m/z* (relative intensity) 465 (M^+, 80), 450 (88), 408 (100), 388 (82), 374 (22), 358 (35), 342 (23); HRMS (ESIMS) calcd for $C_{32}H_{36}NPH^+$ 466.2658, found 466.2622.

[2-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine]palladium(II) dichloride (8d). $Pd(CH_3CN)_2Cl_2$ (5.6 mg, 0.022 mmol) was dissolved in degassed acetonitrile (1 mL) at room temperature under nitrogen. 2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine (pyphos) (**8c**) (10 mg, 0.022 mmol) was then added and the color of the solution was changed from pale yellow to yellow. The reaction mixture was stirred for 5 min at room temperature and the solvent was removed under reduced pressure. The yellow solid was recrystallized in dichloromethane/ether to obtain [2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3-methylpyridine]palladium(II) dichloride (**8d**) (11 mg, 80%) as orange crystals. mp 320°C (decomposed); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.29 (d, 1H, J=3.7 Hz), 7.75 (s, 1H), 7.52–7.55 (m, 2H), 7.27–7.44 (m, 7H), 7.04–7.11 (m, 3H), 6.94–6.99 (m, 2H), 2.20 (s, 3H), 1.24 (s, 9H), 1.09 (s, 9H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 34.15; MS (FAB): *m/z* (relative intensity) 642 (M^++1, 25); HRMS (ESIMS) calcd for $C_{32}H_{36}NPCl_2PdH^+$ 642.1073, found 642.1063. X-Ray crystal was grown under the solvent mixture of dichloromethane/diethyl ether and the X-ray data has been deposited in Cambridge Crystallographic Center (CCDC 147228). Formula: $C_{33}H_{38}Cl_4NPPd$, molecular weight, 727.81, λ=.71073 Å 294(2) K, Crystal: Triclinic, P1; a=10.326 (1) Å, b=10.354 (1) Å, c=16.468 (2) Å; α=95.753 (7)°, β=91.135 (6)°, γ=106.230 (7)°, V=1679.9 (4) Å^3, Z=2, density(calculated)=1.439 Mg/m^3, Crystal Size=0.30×0.25×0.20 mm, reflections collected=5396, independent reflections=5396 (R_{int}=0.0000), data/restraints/parameters=5396/0/362, R Indices (all data): R_1=0.0483, ωR_2=0.1382 [$I>2\sigma(I)$]; R_1=0.0518, ωR_2=0.1439 (all data); GOF=1.063.

3,5-Di-*tert*-butyl-2-(3′,5′-dimethyl-2′-pyridyl)phenyl trifluoromethanesulfonate (9b). The general procedure of trifluoromethanesulfonation for **8b** was used. 3,5-Di-*tert*-butyl-2-(3′,5′-dimethyl-2′-pyridyl)phenol (**9a**) (311 mg, 1.0 mmol), trifluoromethanesulfonic anhydride (0.18 mL, 1.1 mmol), pyridine (0.26 mL, 3.0 mmol), dichloromethane (8 mL) were used to obtain 3,5-di-*tert*-butyl-2-(3′,5′-dimethyl-2′-pyridyl)phenyl trifluoromethanesulfonate (**9b**) (407 mg, 92%) as a white solid. R_f=0.6 (hexane/ethyl acetate=5:1); mp 106–108°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15 (s, 9H), 1.35 (s, 9H), 2.07 (s, 3H), 2.37 (s, 3H), 7.18 (d, 1H, J=1.5 Hz), 7.37 (d, 1H, J=0.6 Hz), 7.60 (d, 1H, J=1.8 Hz), 8.35 (d, 1H, J=1.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.1, 19.1, 31.1, 31.8, 35.1, 37.5, 115.4, 118.2 (q, J_{CF}=317.9) Hz, 124.3, 129.6, 132.6, 133.0, 138.0, 146.6, 148.2, 150.5, 152.3, 152.4; MS (EI): *m/z* (relative intensity) 444 (M^++1, 43), 428 (9), 310 (15), 295 (100); HRMS (ESIMS) calcd for $C_{22}H_{28}F_3NO_3SH^+$ 444.1815, found 444.1804.

2-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3,5-dimethylpyridine (9c). The general procedure of nickel catalyzed phosphination for **8c** was used. 3,5-Di-*tert*-butyl-2-(3′,5′-dimethyl-2′-pyridyl)phenyl trifluoromethanesulfonate (**9b**) (111 mg, 0.25 mmol), bis(triphenylphosphine) nickel(II) chloride (82 mg, 0.13 mmol), chlorodiphenylphosphine (45 μL, 0.25 mmol), Zn (11 mg×3, 0.5 mmol), DMF (1 mL) were used to obtain 2-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-3,5-dimethylpyridine (**9c**) (48 mg, 40%) as a light yellow solid. R_f=0.6 (toluene/ethyl acetate=15:1); mp 111–114°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.13 (s, 9H), 1.17 (s, 9H), 1.89 (s, 3H), 2.35 (s, 3H), 7.05–7.29 (m, 12H), 7.59 (d, 1H, J=2.0 Hz), 8.18 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.2, 19.9, 31.1, 32.4, 34.8, 37.2, 125.8, 127.9, 128.0 (d, J_{CP}=8.0 Hz), 128.2 (d, J_{CP}=4.6 Hz), 130.1, 131.2 (d, J_{CP}=7.6 Hz), 132.1 (d, J_{CP}=7.5 Hz), 133.4 (d, J_{CP}=19.3 Hz), 134.0 (d, J_{CP}=20.0 Hz), 137.1 (d, J_{CP}=8.7 Hz), 138.0 (d, J_{CP}=9.3 Hz), 138.1, 145.1, 147.1 (d, J_{CP}=5.6 Hz), 149.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.78; MS (EI): *m/z* (relative intensity) 479 (M^+, 5), 464 (5), 444 (17), 428 (54), 310 (13), 295 (76), 280 (100); HRMS (ESIMS) calcd for $C_{33}H_{38}NPH^+$ 480.2814, found 480.2807.

3,4,5-Trimethyl-2-(3′-methyl-2′-pyridyl)phenyl trifluoromethanesulfonate (10b). The general procedure of trifluoromethanesulfonation for **8b** was used. 3,4,5-Trimethyl-2-(3′-dimethyl-2′-pyridyl)phenol[17] (**10a**) (250 mg, 1.10 mmol), trifluoromethanesulfonic anhydride (0.20 mL, 1.21 mmol), pyridine (0.27 mL, 3.3 mmol), dichloromethane (6 mL) were used to obtain 3,4,5-trimethyl-2-(3′-methyl-2′-pyridyl)phenyl trifluoromethanesulfonate (**10b**) (355 mg, 90%) as a white solid. R_f=0.5 (hexane/ethyl acetate=4:1); mp 64–66°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.99 (s, 3H), 2.10 (s, 3H), 2.23 (s, 3H), 2.37 (s, 3H), 7.05 (s, 1H), 7.26 (dd, 1H, J=8.2, 3.9 Hz), 7.63 (d, 1H, J=7.7 Hz), 8.56 (d, 1H, J=4.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.1, 18.4, 20.9, 29.7, 116.0, 118.2 (q, J_{CF}= 317.8 Hz), 124.5, 130.8, 133.1, 136.1, 137.1, 137.9, 138.3, 144.6, 147.0, 153.9; MS (EI): *m/z* (relative intensity) 359 (M^+, 42), 344 (66), 226 (79), 211 (100), 196 (16), 182 (19); HRMS (ESIMS) calcd for $C_{16}H_{16}F_3NO_3SH^+$ 360.876, found 360.878.

2-(2′-Diphenylphosphino-4′,5′,6′-trimethyl-1′-phenyl)-3-methylpyridine (10c). The general procedure of nickel

catalyzed phosphination for **8c** was used. 3,4,5-Trimethyl-2-(3′-methyl-2′-pyridyl)phenyl trifluoromethanesulfonate (**10b**) (90 mg, 0.25 mmol), bis(triphenylphosphine) nickel (II) chloride (82 mg, 0.13 mmol), chlorodiphenylphosphine (45 μL, 0.25 mmol), Zn (11 mg×3, 0.5 mmol), DMF (1 mL) were used to obtain 2-(2′-diphenylphosphino-4′,5′,6′-trimethyl-1′-phenyl)-3-methylpyridine (**10c**) (38 mg, 38%) as a white solid. R_f=0.4 (toluene/ethyl acetate=15:1); mp 100–102°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.90 (s, 3H), 1.97 (s, 3H), 2.20 (s, 3H), 2.21 (s, 3H), 6.79 (d, 1H, *J*=4.0 Hz), 7.12–7.28 (m, 11H), 7.51 (d, 1H, *J*=7.6 Hz), 8.32 (d, 1H, *J*=4.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.9, 16.9, 19.0, 20.9, 122.2, 128.0 (d, J_{CP}=7.1 Hz), 128.2 (d, J_{CP}=7.2 Hz), 132.2 (d, J_{CP}=9.3 Hz), 132.7 (d, J_{CP}=13.4 Hz), 132.8, 133.4 (d, J_{CP}=19.1 Hz), 133.8 (d, J_{CP}=20.0 Hz), 136.2, 136.9, 137.2 (d, J_{CP}=10.8 Hz), 137.4, 137.7 (d, J_{CP}=11.6 Hz), 146.1, 159.6 (d, J_{CP}=5.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.53; MS (EI): *m*/*z* (relative intensity) 395 (M^+, 100), 379 (25), 334 (9), 318 (66); HRMS (ESIMS) calcd for $C_{27}H_{26}NPH^+$ 396.1876, found 396.1886.

3,5-Di-*tert*-butyl-2-(2′-isoquinolyl)phenyl trifluoromethanesulfonate (11b). The general procedure of trifluoromethanesulfonation for **8b** was used. 3,5-Di-*tert*-butyl-2-(2′-isoquinolyl)phenol[17] (**11a**) (50 mg, 0.15 mmol), trifluoromethanesulfonic anhydride (28 μL, 0.17 mmol), pyridine (36 μL, 0.45 mmol), dichloromethane (2 mL) were used to obtain 3,5-di-*tert*-butyl-2-(2′-isoquinolyl)phenyl trifluoromethanesulfonate (**11b**) (62 mg, 89%) as a white solid. R_f=0.5 (hexane/ethyl acetate=5:1); mp 78–80°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.07 (s, 9H), 1.40 (s, 9H), 7.27 (s, 1H), 7.47–7.56 (m, 2H), 7.64–7.71 (m, 3H), 7.87 (d, 1H, *J*=8.2 Hz), 8.62 (d, 1H, *J*=5.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.1, 32.2, 35.2, 37.6, 115.5, 117.9 (q, J_{CF}=317.9 Hz), 120.7, 124.3, 126.8, 127.0, 127.3, 128.4, 129.3, 130.2, 135.8, 141.7, 148.5, 151.3, 153.1, 157.3; MS (EI): *m*/*z* (relative intensity) 465 (M^+, 100), 450 (37), 422 (11), 407 (7), 332 (64), 316 (32); HRMS (ESIMS) calcd for $C_{24}H_{26}F_3NO_3SH^+$ 466.1658, found 466.1652.

1-(2′-Diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)-isoquinoline (11c). The general procedure of nickel catalyzed phosphination for **8c** was used. 3,5-Di-*tert*-butyl-2-(2′-isoquinolyl)phenyl trifluoromethanesulfonate (**11b**) (116 mg, 0.25 mmol), bis(triphenylphosphine) nickel(II) chloride (82 mg, 0.13 mmol), chlorodiphenylphosphine (45 μL, 0.25 mmol), Zn (11 mg×3, 0.5 mmol), DMF (1 mL) were used to obtain 1-(2′-diphenylphosphino-4′,6′-di-*tert*-butyl-1′-phenyl)isoquinoline (**11c**) (51 mg, 41%) as a white solid. R_f=0.5 (toluene/ethyl acetate=15:1); mp 144–146; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (s, 9H), 1.23 (s, 9H), 6.94 (t, 1H, *J*=8.2 Hz), 7.06–7.27 (m, 11H), 7.49 (t, 1H, *J*=8.0 Hz), 7.64 (d, 1H, *J*=5.7 Hz), 7.68 (d, 1H, *J*=1.9 Hz), 7.78 (d, 1H, *J*=8.2 Hz), 8.51 (d, 1H, *J*=5.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.2, 32.7, 34.9, 37.3, 120.0, 125.6, 126.1, 126.4, 127.9 (d, J_{CP}=18.0 Hz), 128.0, 128.2 (d, J_{CP}=18.2 Hz), 129.5, 130.2, 130.4 (d, J_{CP}=5.0 Hz), 133.1 (d, J_{CP}=18.9 Hz), 133.7 (d, J_{CP}=20.6 Hz), 135.8, 137.9 (d, J_{CP}=15.0 Hz), 138.4 (d, J_{CP}=15.0 Hz), 141.2, 147.8 (d, J_{CP}=5.9 Hz), 150.0, 163.6 (d, J_{CP}=6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.23; MS (EI): *m*/*z* (relative intensity) 501 (M^+, 70), 474 (7), 460 (11), 424 (100), 407 (23), 392 (21), 375 (10); HRMS (ESIMS) calcd for $C_{35}H_{37}NPH^+$ 502.2658, found 502.2646.

1-(2′-Isoquinolyl)naphthyl trifluoromethanesulfonate (12b). The general procedure of trifluoromethanesulfonation for **8b** was used. 1-(2′-Hydroxy-1′-naphthyl)isoquinoline[3a] (**12a**) (250 mg, 0.92 mmol), trifluoromethanesulfonic anhydride (0.17 mL, 1.01 mmol), pyridine (0.22 mL, 2.77 mmol), dichloromethane (6 mL) were used to obtain 1-(2′-isoquinolyl)naphthyl trifluoromethanesulfonate (**12b**) (334 mg, 90%) as a light yellow solid. R_f=0.6 (hexane/ethyl acetate=4:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (d, 1H, *J*=8.5 Hz), 7.40 (t, 1H, *J*=7.7 Hz), 7.49–7.43 (m, 2H), 7.57 (t, 1H, *J*=7.6 Hz), 7.62 (d, 1H, *J*=9.1 Hz), 7.72 (m, 1H), 7.85 (d, 1H, *J*=5.7 Hz), 7.97 (d, 1H, *J*=8.3 Hz), 8.00 (d, 1H, *J*=8.3 Hz), 8.11 (d, 1H, *J*=9.1 Hz), 8.79 (d, 1H, *J*=5.7 Hz); MS (EI): *m*/*z* (relative intensity) 403 (M^+, 80), 254 (100), 128 (12), 126 (21).

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