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Research Paper

Development of highly electron-deficient and less sterically-hindered phosphine ligands possessing 1,3,5-triazinyl groups

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ABSTRACT

Highly electron-deficient and less sterically-hindered phosphine ligands with two or three 1,3,5-triazinyl groups on the phosphorus atoms have been synthesized and examined in transition metal-catalyzed reactions for the first time. Due to the lack of any hydrogens or substituents at *ortho*-positions of the 1,3,5-triazine towards the phosphorous atom, it is considered that the steric hindrance of the tris(triazinyl)phosphine ligand to a metal center is *least* among triarylphosphine ligands. In the Stille coupling of aryl iodides, these electron-poor phosphine ligands provided good product yields compared to hitherto well-known phosphine ligands.

1. Introduction

Electron-rich phosphines have been widely used as ligands in transition metal catalysts for controlling the catalytic activity because they promote the oxidative addition of metals. In contrast, electron-poor ligands are believed to accelerate the reductive elimination, transmetalation, and insertion reactions [1]. In fact, several types of electron-deficient P-containing ligands that exhibit prominent ligand effects have been developed. For example, phosphinite-, phosphonite-, and phosphite-containing electronegative *O*-substituents have been used [2]. However, the P—O bonds of these compounds occasionally undergo hydrolysis [2e,2f]. Consequently, electron-poor phosphine ligands having stable P—C bonds, such as fluoroarylphosphines [1,3] and α-cationic phosphines [4], have also been studied. One example of this is commercially available tris(pentafluorophenyl)phosphine [$P(C_6F_5)_3$, Fig. 1]; however, its *ortho*-fluorine atoms destabilize the metal–phosphorus bond and can occasionally cause the decomposition of the metal complex due to the steric hindrance [1,5]. To overcome this issue, Korenaga and Sakai prepared electron-poor phosphines with 2,6-bis(trifluoromethyl)-4-pyridyl (BFPy) groups whose steric hindrance at the *ortho*-positions (hydrogens) was less than that of the pentafluorophenyl group (Fig. 1) [1].

In our laboratory, we investigated a variety of synthetic reagents that are based on 1,3,5-triazine for the dehydrative condensing reactions [6] or *O*-alkylations [7]. Some important characteristics of 1,3,5-triazine are its highly π-electron-deficient property [8] and the lack of substituents on the three nitrogens of the triazine ring. The steric hindrance around the nitrogen atoms should be minimal [8,9][8b,9]; thus, we expected that 1,3,5-triazin-2-yl phosphines could be useful electron-deficient and less sterically-hindered ligands for metal catalysts. In addition, 1,3,5-triazine have great potential as a supramolecular component owing to their non-covalent bonds, which involve either its nitrogen lone pairs (coordination to metals and hydrogen bonds) or its heteroaromatic π-electrons ("cation–π interactions," "anion–π interactions," and "π–π stacking interactions") [10]. Therefore, it was anticipated that these non-covalent bonds could afford novel reactivity for metal catalysts. However, to the best of our knowledge, there have been a few reports on the reactions using triazinylphosphines as metal ligands, all of which were limited to mono(triazinyl)phosphines [11], possibly because of the lack of facile triazinylphosphine synthesis methods. In the reported synthesis procedures, triazinylphosphines were prepared by the reaction of nucleophilic phosphorus reagents, such as R_2PSiMe_3 and R_2PM (M = Li, Na, and K), with electrophilic triazine compounds, such as chlorotriazine derivatives [11,12]. Because chlorotriazines are known to readily undergo nucleophilic aromatic substitution, the synthetic methods for the preparation of the triazinylphosphines reported to date typically employ nucleophilic phosphorous compounds.

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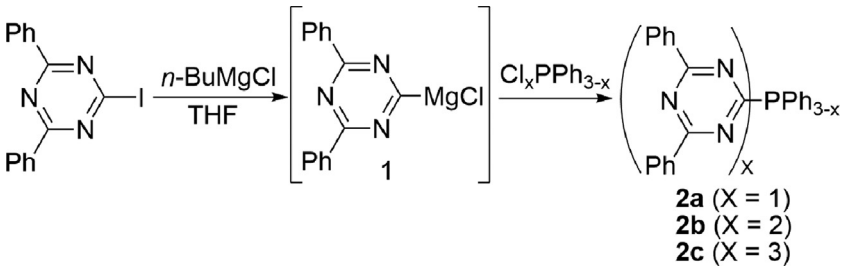
2468-8231/



Scheme 1. Synthesis of mono-, bis-, and tris(triazinyl)phosphines.

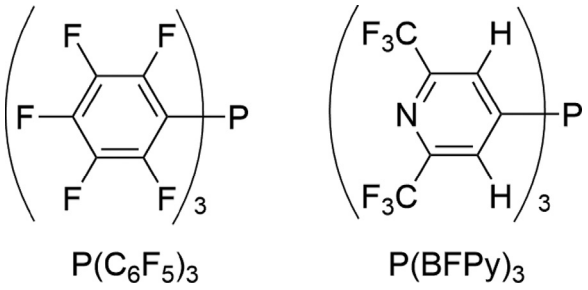


Fig. 1. Chemical structures of previously reported phosphine ligands.

However, the execution of such procedures for synthesizing bis- and tris(triazinyl)phosphines is difficult because the nucleophilicity of phosphines will decrease with an increase in the number of electron-withdrawing triazinyl groups on phosphorous atoms [13]. Herein, we report the development of a practical method for the synthesis of mono-, bis-, and tris(triazinyl)phosphines (**2a**–**2c** in Scheme 1) and the use of these phosphines as ligands in Stille coupling.

2. Experimental section

2.1. General information

Nuclear magnetic resonance spectra were determined on a JEOL JNM-ECS400 spectrometer [^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), ^{31}P NMR (162 MHz)]. Chemical shifts for ^{1}H NMR are reported as δ values relative to tetramethylsilane as an internal standard and coupling constants are in hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Chemical shifts for ^{13}C NMR were reported in ppm relative to the center line of a triplet at 77.16 ppm for deuteriochloroform. Chemical shifts for ^{31}P NMR are reported as δ values relative to 85% H_3PO_4 as an external standard. Mass spectra were measured on a JMS-T100TD AccuTOF TLC (DART-MS, ESI–MS), JMS-SX102A (FAB-MS, EI-MS). Infrared (IR) spectra were recorded on a HORIBA FT-720 spectrometer and are reported in wavenumbers (cm^{-1}). GC analysis was carried out using SHIMADZU GC-17A equipped with AGILENT TECHNOLOGIES DB-5 capillary column (length 30 m, 0.32 mm I.D.). Analytical TLC was performed on Merck precoated analytical plates, 0.25 mm thick, silica gel 60 F_{254}. Flash chromatography separations were performed on SiO_2 [KANTO CHEMICAL Silica Gel 60 N (spherical, neutral, 40–100 mesh)] or SiO_2/K_2CO_3 (9:1, w/w) [14]. Reagents were commercial grades and were used without any purification unless otherwise noted. Tetrahydrofuran (THF) was distilled over sodium/benzophenone ketyl before use. All reactions sensitive to oxygen or moisture were conducted under a N_2 atmosphere.

2.2. Experimental procedures and characterization data for the phosphine ligands

2.2.1. Diphenyl(4,6-diphenyl-1,3,5-triazin-2-yl)phosphine (**2a**)

To a solution of 2-iodo-4,6-diphenyl-1,3,5-triazine [15] (860.0 mg, 2.39 mmol) in THF (8.0 mL), *n*-butylmagnesium chloride (1.45 M solution in THF, 2.0 mL, 2.90 mmol) was added dropwise at −78 °C. After the reaction mixture was stirred for 1 h at −78 °C, distilled chlorodiphenylphosphine (0.53 mL, 2.87 mmol) was added dropwise. The reaction mixture was allowed to warm to room temperature and stirred for 2 h, followed by quenching with sat. aq. NH_4Cl (0.4 mL). Subsequently, Et_2O (30 mL) was added. The resulting mixture was filtered through a Celite pad and the filtrate was evaporated. The residue was purified by column chromatography (hexane:toluene = 75:25) to afford **2a** (839.3 mg, 84%) as a white solid.

Mp: 132–133 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52–8.47 (m, 4H), 7.70–7.62 (m, 4H), 7.54 (t, J = 7.3 Hz, 2H), 7.50–7.39 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.0 (d, J_{C-P} = 6.7 Hz), 169.7 (d, J_{C-P} = 4.8 Hz), 136.0, 135.0 (d, J_{C-P} = 19.2 Hz), 134.4 (d, J_{C-P} = 6.7 Hz), 132.7, 129.5, 129.1, 128.7, 128.5 (d, J_{C-P} = 7.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 1.49; HRMS (EI) Calcd for $C_{27}H_{20}N_3P$ ($[M]^+$): 417.1395, Found: 417.1400; Anal. Calcd for $C_{27}H_{20}N_3P$: C, 77.68; H, 4.83; N, 10.07. Found: C, 77.38; H, 4.71; N, 10.00; IR (KBr): 3053, 1599, 1585, 1516, 1495, 1437, 1354, 1254, 1173, 1024, 833, 756, 692, 644 cm^{-1}.

2.2.2. Bis(4,6-diphenyl-1,3,5-triazin-2-yl)phenylphosphine (**2b**)

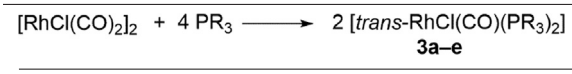
Compound **2b** was prepared in a manner same as that of **2a** using 2-iodo-4,6-diphenyl-1,3,5-triazine [15] (1.98 g, 5.51 mmol), *n*-butylmagnesium chloride (1.45 M solution in THF, 3.6 mL, 5.22 mmol), distilled dichlorophenylphosphine (0.33 mL, 2.43 mmol), and THF (18.4 mL). The crude product was purified by column chromatography (hexane:toluene = 60:40) to yield **2b** (1.02 g, 73%) as a white solid.

Mp: 212–214 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54–8.50 (m, 8H), 7.95–7.89 (m, 2H), 7.59–7.48 (m, 7H), 7.43 (t, J = 7.6 Hz, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.6 (d, J_{C-P} = 12.5 Hz), 170.1 (d, J_{C-P} = 5.8 Hz), 137.1 (d, J_{C-P} = 22.0 Hz), 135.8, 132.7, 131.4 (d, J_{C-P} = 3.8 Hz), 130.7, 129.2, 128.7, 128.5 (d, J_{C-P} = 9.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ 4.62; HRMS (EI) Calcd for $C_{36}H_{25}N_6P$ ($[M]^+$): 572.1878, Found: 572.1873; Anal. Calcd for $C_{36}H_{25}N_6P$: C, 75.51; H, 4.40; N, 14.68. Found: C, 75.54; H, 4.51; N, 14.35; IR (KBr): 3059, 1599, 1585, 1502, 1439, 1390, 1356, 1319, 1255, 1173, 1026, 837, 756, 690, 644 cm^{-1}.

2.2.3. Tris(4,6-diphenyl-1,3,5-triazin-2-yl)phosphine (**2c**)

To a solution of 2-iodo-4,6-diphenyl-1,3,5-triazine [15] (2.95 g, 8.21 mmol) in THF (27.0 mL), *n*-butylmagnesium chloride (1.45 M solution in THF, 5.5 mL, 7.98 mmol) was added dropwise at −78 °C. After the mixture was stirred for 1 h at −78 °C, distilled phosphorus trichloride (0.21 mL, 2.40 mmol) was added dropwise. The reaction mixture was allowed to warm to room temperature and stirred for

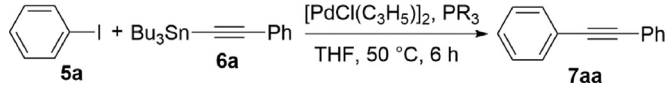
Table 1
Evaluation of the electronic properties of triazinylphosphines (**2a–c**) using ^{31}P NMR spectra, IR spectra, and X-ray single-crystal structure analysis.



3 (PR_3)	ν^{CO} (cm^{-1})[a]	J_{Rh-P} (Hz) [δ (ppm)][b]	Rh—P bond length (Å)[c]
3c (**2c**)	2006	145.2 [44.0]	2.295[d]
3b (**2b**)	1996	140.9 [42.7]	2.292[d]
3a (**2a**)	1986	130.0 [34.3]	2.323[d]
3d [P(2-furyl)$_3$]	1998	130.0 [−23.9]	2.303[d,e]
3e (PPh_3)	1979	127.9 [29.6]	2.325[e,f]

[a] IR spectra in CH_2Cl_2.
[b] ^{31}P NMR spectra in $CDCl_3$.
[c] From X-ray single-crystal structure analysis.
[d] Obtained from this study (refer to the Supplementary data).
[e] The mean value of two Rh—P bonds.
[f] From reference [20].

Table 2
Stille coupling of **5a** with **6a** by using various phosphine ligands.



Entry	$[PdCl(C_3H_5)]_2$ (mol%)	PR_3	P:Pd	Yield of **7aa** (%)[a]
1	2.5	**2a**	2:1	21
2	2.5	**2b**	2:1	79
3	2.5	**2c**	2:1	92
4	2.5	P(2-furyl)$_3$	2:1	80
5	2.5	PPh_3	2:1	35
6	2.5	–	–	28
7	1.0	**2c**	2:1	91 (86)
8	1.0	**2c**	1:1	90
9	1.0	**2c**	3:1	83

[a] Yields were determined by ^{1}H NMR; isolated yield is shown in parentheses.

3 h, followed by quenching with sat. aq. NH_4Cl (0.8 mL). The precipitate was collected using a centrifuge, successively washed with THF, water, MeOH, and THF, and dried in vacuo to yield **2c** (1.10 g, 63%) as a white solid. ^{13}C NMR was measured at 50 °C because of its low solubility. For HRMS measurement, $[PdCl(C_3H_5)]_2$ was added into the sample solution to dissolve **2c**.

Mp: >300 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55–8.50 (m, 12H), 7.53–7.48 (m, 6H), 7.38 (t, J = 7.6 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$, 50 °C): δ 182.1 (d, J_{C-P} = 15.3 Hz), 170.5 (d, J_{C-P} = 5.8 Hz), 135.9, 132.8, 129.3, 128.7; ^{31}P NMR (162 MHz, $CDCl_3$): δ 9.01; HRMS (FAB) Calcd for $C_{45}H_{31}N_9P$ ([M+H]$^+$): 728.2440, Found: 728.2438; Anal. Calcd for $C_{45}H_{30}N_9P{\cdot}3H_2O$: C, 69.13; H, 4.64; N, 16.12. Found: C, 69.25; H, 4.36; N, 16.11 (In the IR spectrum, a signal for water was observed.); IR (KBr): 3402, 3068, 1601, 1585, 1504, 1439, 1394, 1358, 1317, 1254, 1173, 1024, 839, 758, 692, 644 cm^{-1}.

2.3. X-ray single-crystal structure analysis of the rhodium complexes (*3a–d*) and the palladium complex (*4c*)

The rhodium complexes (**3a**–**e**) and the palladium complex (**4c**) were prepared from $[RhCl(CO)_2]_2$ or $[PdCl(C_3H_5)]_2$ and corresponding phosphine ligands (refer to the Supplementary data for details). Measurements for X-ray single-crystal structure analysis were made on a Rigaku R-AXIS RAPID diffractometer using graphite monochromated Mo-Kα radiation at −170 °C. The structures were solved by direct methods [16] and refined by SHELXL [17]. For **3b**, **3c**, and **4c**, PLATON SQUEEZE [18] was used for disordered solvents. CCDC 1552090 (**3c**), CCDC 1552091 (**3b**), CCDC 1552092 (**3a**), CCDC 1552093 (**3d**), and CCDC 1552094 (**4c**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

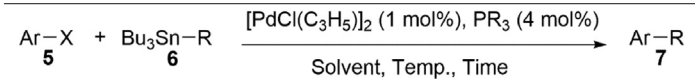
2.4. General experimental procedure for the Stille coupling reactions

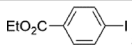
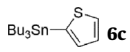
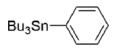
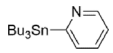
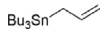
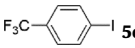
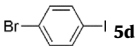
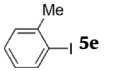
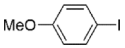
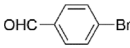
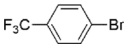
To the mixture of a phosphine ligand (8.8 μmol) and $[PdCl(C_3H_5)]_2$ (0.8 mg, 2.2 μmol) in the appropriate solvent (2.5 mL), a hydrocarbon (0.22 mmol, an internal standard for GC analysis), aryl halide (0.22 mmol), and organostannane (0.24 mmol) were added. The reaction mixture was stirred at the appropriate temperature until GC or TLC analysis indicated the consumption of the starting materials. Subsequently, the mixture was diluted with Et_2O and washed with H_2O and brine. The organic extracts were dried over anhydrous sodium sulfate and filtered. The solvent was removed by rotary evaporation, and the residue was purified by column chromatography (SiO_2/K_2CO_3 (9:1, w/w)) to afford the coupling product **7**.

3. Results and discussion

Because of the aforementioned reasons, we chose to react electrophilic phosphines, such as phosphorus halides, with nucleophilic 1,3,5-triazinylmagnesium reagents. Although various functional groups can be generally introduced into the 4,6-positions of the 1,3,5-triazin-2-yl group, e.g., the amino and alkoxy groups, these types of functional groups are not suitable because they may be replaced by strongly nucleophilic Grignard reagents. Thus, we employed a triazinylmagnesium reagent (**1**) with a carbon substituent, i.e., a phenyl group, at the 4,6-positions [15]. From the reaction of **1** with chlorophosphines possessing different numbers of chloro substituents [Cl_xPPh_{3-x} (X = 1, 2, or 3)], we successfully synthesized mono-, bis-, and tris(diphenyltriazinyl)phosphines (**2a**–**c**) in 84%, 73%, and 63% yields, respectively (Scheme 1). All compounds were stable solids. Compounds **2a** and **2b** were solu-

Table 3
Stille coupling reactions of various starting materials.



Entry	Ar – X (5)	Bu_3Sn – R (6)	Solvent	Temp. (°C)	Time (h)	Yield of **7** (%)[a]				
						2c	**2b**	**2a**	P(2-furyl)$_3$	PPh_3
1	 **5b**	**6a**	THF	50	3	91 (89)	60	13	67	11
2	**5b**	 **6b**	THF	50	10	91 (88)	74	66	42	39
3	**5b**	 **6c**	toluene	90	1.5	99 (quant.)	42	15	50	8
4[b]	**5b**	 **6d**	toluene	90	9	91 (89)	74	20	50	11
5[c]	**5b**	 **6e**	toluene	90	7	82 (78)	87	90	84	48
6[d]	**5b**	 **6f**	toluene	Reflux	21	46	56	81 (78)	39	90
7	 **5c**	**6a**	THF	RT	24	93 (90)	95	64	75	73
8	 **5d**	**6a**	THF	50	3	83[e] (83)	59[e]	12[e]	58[e]	8[e]
9	 **5e**	**6a**	THF	50	6	67 (66)	68	59[f]	63	20[f]
10	 **5f**	**6a**	THF	50	5	52 (43)	51	12	50	14
11	 **5g**	**6a**	toluene	90	1.5	30	69	90 (83)	52	96
12	 **5h**	**6a**	toluene	90	1	6[e]	30[e]	75[e] (83)	20[e]	72[e]
13	 **5i**	**6a**	toluene	90	24	(40)	(48)	(56)	(36)	(67)
14	 **5j**	**6a**	toluene	90	2.5	40	65	82 (76)	84	72

[a] Yields were determined by ^{1}H NMR unless otherwise noted; isolated yields are shown in parentheses.
[b] Tributylphenyltin (**6d**, 1.3 eq.) was used.
[c] Tributyl(2-pyridyl)tin (**6e**, 1.3 eq.) was used.
[d] Allyltributyltin (**6f**, 1.3 eq.), $[PdCl(C_3H_5)]_2$ (2.5 mol%), and PR_3 (10 mol%) were used.
[e] Determined by GC analysis.
[f] Reaction time was 24 h.

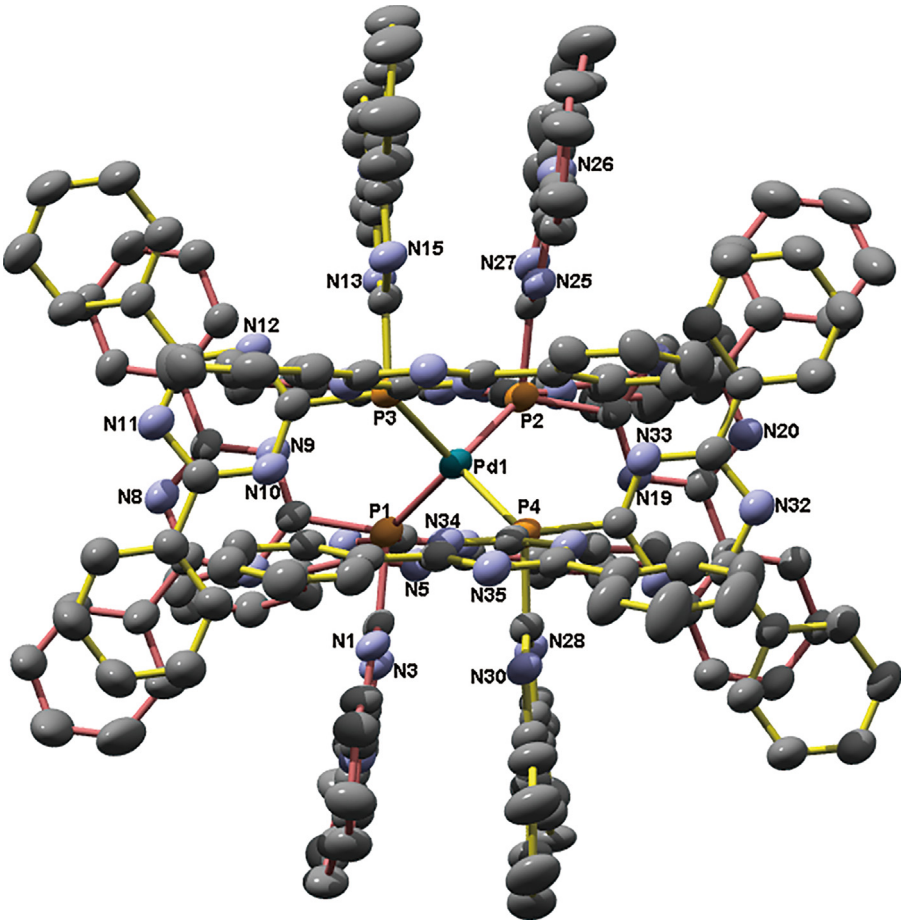


Fig. 2. X-ray crystal structure of complex **4c** [Pd(0)(**2c**)$_4$]. Thermal ellipsoids drawn at 50% probability and hydrogen atoms are omitted for clarity. For details, refer to the Supplementary data.

ble in common organic solvents, while **2c** exhibited low solubility, which may have been due to the high co-planarity [9] of the diphenyltriazinyl moiety, which may increase the product's ability to crystallize.

The electronic properties of these triazinylphosphines (**2a**–**c**) were evaluated by the ^{31}P NMR spectroscopy and the IR spectroscopy of the corresponding rhodium complexes, i.e., *trans*-RhCl(CO)(PR$_3$)$_2$ [19]. Both the J_{Rh-P} value of the ^{31}P NMR spectrum and the ν^{CO} value in IR spectrum of the complex generally increase with an increase in the electron-withdrawing capability of the phosphine (PR$_3$). As anticipated for the complexes (**3a**–**c**) comprising **2a**–**c**, the order of the J_{Rh-P} values was **3c** >**3b** >**3a** (Table 1). Compared to the well-known phosphines tri(2-furyl)phosphine [P(2-furyl)$_3$] and PPh$_3$, **3a** had a value similar to the values of these compounds, while **3c** and **3b** resulted in larger coupling constants. Similarly, the ν^{CO} values also indicated that **3c** and **3b** possessed a high electron-withdrawing character.

Moreover, the Rh—P bond lengths determined by single-crystal X-ray structure analysis also implied similar electronic properties (Table 1, Fig. S1–S4, S6–S7, and Table S1 in the Supplementary data). The order of the bond lengths was **3c** ≈ **3b** < **3a** [21], indicating that the higher electron-withdrawing character of the phosphines shortened their bond lengths. This tendency in the Rh—P bond lengths has also been observed in other rhodium complexes (Fig. S6 in the Supplementary data). Furthermore, a linear relationship between their bond lengths and the σ_p Hammett constants of the substituents on phosphines was observed (Fig. S7 in the Supplementary data).

In addition, we successfully obtained a crystal structure of the palladium complex **4c** [Pd(0)(**2c**)$_4$] generated using one equivalent of [PdCl(C$_3$H$_5$)]$_2$ and four equivalents of **2c** (phosphine:palladium ratio = 2:1; Fig. 2 and Fig. S5 in the Supplementary data). Due to the minimal steric hindrance of the nitrogen atoms, the diphenyltriazinyl moieties were nearly coplanar [9] and the π–π stacking interactions were observed between these moieties that are from two different **2c**. Thus, it was expected that these monodentate **2c** could function as a bidentate-like ligand through their non-covalent bonds [22]. As can be observed in the Rh complexes, the averaged Pd—P bond length of **4c** was shorter than that of Pd(PPh$_3$)$_4$ [2.305 Å for **4c**, 2.450 Å [23] for Pd(PPh$_3$)$_4$].

The ligand effect of the triazinylphosphines (**2a**–**c**) in a model catalytic reaction was examined using the Stille coupling reaction, the rate-determining step of which is known to be the transmetalation of organostannanes with palladium complexes [3f,24]. Stille coupling with iodobenzene is more successful when performed using less σ-donating ligands, such as P(2-furyl)$_3$ and triphenylarsine, because these ligands easily provide a vacant coordination site for organostannanes.

First, we conducted the Stille coupling of iodobenzene (**5a**) with tributyl(phenylethynyl)tin (**6a**) in the presence of 2.5 mol% [PdCl(C$_3$H$_5$)]$_2$ and 10 mol% phosphine ligands (Table 2, entries 1–5) and the time course of product yields of the reactions using each ligand is shown in Fig. S8 (the supplementary data). In the reactions using ligands **2a**–**c**, the yields of **7aa** and rate of reactions increased with the number of triazinyl groups (Table 2, entries 1–3 and Fig. S8 in the supplementary data). In particular, **2c**, which had the three triazinyl substituents, resulted in a higher yield compared to P(2-

furyl)$_3$ (Table 2, entries 3 vs. 4). Although **2c** was sparingly soluble in THF, a mixture of **2c** and [PdCl(C_3H_5)]$_2$ was more soluble. This result suggested that **2c** coordinates with Pd to form the **2c**–Pd complex, which is soluble in THF. In the absence of the phosphine ligand, the reaction resulted in a decreased yield of **7aa** (Table 2, entry 6). Both the amount of [PdCl(C_3H_5)]$_2$ and **2c** could be reduced to 1 mol% and 4 mol%, respectively, without a loss in the product yield (Table 2, entry 7). The yield of the product was slightly lower when the phosphine:palladium (P:Pd) ratio was 3:1 rather than 2:1 and 1:1 (Table 2, entries 7 and 8 vs. 9). This result may indicate that additional **2c** interferes with the coordination of the substrate to Pd. Moreover, the turnover numbers (TON) and turnover frequencies (TOF) were determined for **2c** (4400 and 370 h^{-1}) and **2b** (4300 and 360 h^{-1}), respectively (0.005 mol% of [PdCl(C_3H_5)]$_2$ and 0.04 mol% of the ligands were used and the reaction time was 12 h). From these findings, we investigated the Stille coupling reaction of other substrates using 1 mol% [PdCl(C_3H_5)]$_2$ and 4 mol% of the triazinylphosphine ligands. The PPh_3 and P(2-furyl)$_3$ ligands were also examined for comparison.

The Stille coupling of several types of organostannanes (**6a**–**f**) with ethyl 4-iodobenzoate (**5b**) was also investigated (Table 3, entries 1–6). The order of the transmetalation rate of the organostannanes is known to be alkynyl > alkenyl > aryl > allyl ≈ benzyl » alkyl [25]. With the most reactive organostannanes (**6a** and **6b**) in THF at 50 °C, the product yields increased with an increase in the number of triazinyl groups on the phosphines (**2a**–**c**), while PPh_3 or P(2-furyl)$_3$ produced low-to-moderate product yields (Table 3, entries 1 and 2). Similarly, ligand **2c** afforded the best results for the reaction with moderately reactive aryltin compounds **6c** and **6d** at a higher temperature (90 °C) in toluene (Table 3, entries 3 and 4). No significant difference in the ligand effect (except when using PPh_3) was observed in the reaction employing tributyl(2-pyridyl)tin (**6e**; Table 3, entry 5). The reaction of less reactive allyltributyltin (**6f**) required harsher conditions (under reflux of toluene for 21 h), and the ligand effect was reversed compared to the reactions of the other organostannanes (**6a**–**e**), i.e., less electron-deficient PPh_3 and **2a** afforded good yields (Table 3, entry 6).

The coupling results of other aryl halides (**5c**–**j**) with **6a** are shown in entries 7–14 (Table 3). For aryl iodides **5c** or **5d** (possessing *p*-(trifluoromethyl) or *p*-bromo substituents, respectively), ligand **2c** resulted in the high product yields (Table 3, entries 7 and 8). In particular, the coupling of **5d** selectively proceeded at the site of the more reactive iodo-substituent with the bromo-substituent remaining intact. When the reactions of aryl iodides comprising electron-donating groups, such as *ortho*-methyl group (**5e**) or *para*-methoxy group (**5f**), were conducted, the product yields were generally moderate or low; however, the use of ligands **2b** and **2c** resulted in better yields (Table 3, entries 9 and 10). Because organostannane **6a** disappeared and aryl iodides **5e** and **5f** remained in the reaction solution at the end of the reactions, decomposition of **6a** could occur during slow transmetalation between **6a** and a Pd complex intermediate. In the reactions of aryl bromides (**5g**–**j**), the order of the ligand effect was reversed compared to the reaction of aryl iodides, i.e., the higher yields were obtained with the more electron-rich ligands (Table 3, entries 11–14). In the case of aryl bromides, the rate-determining step will probably change from the transmetalation step to the oxidative addition step.

4. Conclusions

We successfully developed a practical method for the synthesizing mono-, bis-, and tris(triazinyl)phosphines **2a**–**c** by reacting chlorophosphines with triazinylmagnesium halide. In addition, we found that the highly π-electron-deficient ligands **2c** or **2b** (which comprise three or two triazinyl groups, respectively, on the phosphorus atoms) provided good results for the Stille coupling reaction of aryl iodides. Ligands **2c** and **2b** may be effective for other metal-catalyzed reactions in which transmetalation, insertion, or reductive elimination is the rate-determining step. Because various functional aryl groups can be readily introduced into the 4,6-positions of the triazine ring, the electronic and steric properties of triazinylphosphine can be finely tuned, providing phosphine ligands with new functionalities. We believe that these triazinylphosphine ligands will exhibit different reactivity for metal-catalyzed reactions due to the non-covalent bonds of 1,3,5-triazine.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.mcat.2017.11.008.

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