

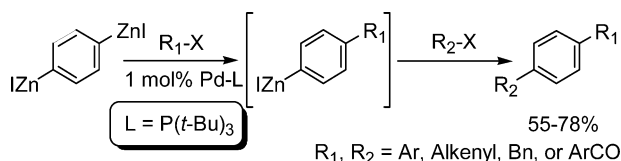
Pd–P(*t*-Bu)₃-Catalyzed Consecutive Cross-Coupling of *p*-Phenylenedizinc Compound with Two Different Electrophiles Leading to Unsymmetrically 1,4-Disubstituted Benzenes

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Pd–P(*t*-Bu)₃ was found to be a *chemoselective* catalyst for the reaction of *p*-phenylenedizinc compound with equimolar amounts of carbon electrophiles to afford the single cross-coupling products in good yields, effectively suppressing the formation of double cross-coupling products. The subsequent additions of other electrophiles to the resulting solutions caused the second cross-coupling of the incipient products to take place, achieving a novel and efficient one-pot synthesis of unsymmetrically 1,4-disubstituted benzenes. The origin of the observed high chemoselectivity was speculated.

As a synthetic method of disubstituted benzenes **1**, the cross-coupling reaction between phenylene-supplying reagents **2**, synthetic equivalents of **3a–c**, and their electronically matching counterparts is useful, since the products are entirely free from contamination by any regioisomers (Figure 1).¹ In the reaction, the consecutive treatment of **2** with two kinds of coupling

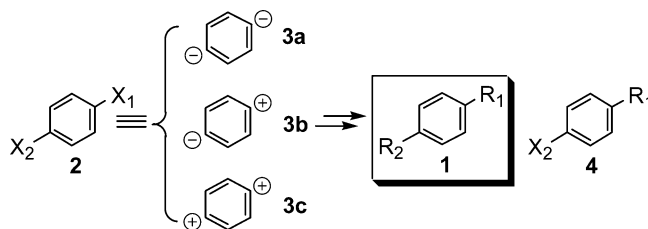


FIGURE 1. Synthesis of *p*-disubstituted benzenes.

partners provides **1** with an unsymmetrical structure, in which the greater the difference in reactivity between the two leaving groups *X*₁ and *X*₂, the higher the degree of selectivity in the transformation of **2** to the desired product. Thus, in such reactions, the synthetic equivalents of **3b** (possessing *X*₁ = I or Br and *X*₂ = B, Zn, Mg, or Sn²) or **3c** (possessing *X*₁ = I and *X*₂ = Br or OTf³) have been generally employed, whereas those of **3a** have been little utilized, presumably because of the difficulty in preparing **2** with two different kinds of electrofuges.⁴ Hereupon, it is noted that, even if the electrofuges are the same, i.e., *X*₁ = *X*₂, the chemoselective coupling on one site is essentially possible; the reactivity of the singly coupled product **4** is no longer the same as that of the starting material. Thus far, the transformations using the synthetic equivalents of **3a** have been carried out using B or Sn derivatives along with the catalysis by Pd, thus affording unsymmetrical terphenyls in the low yields of 13–33% by the consecutive treatment with two kinds of aryl iodides.^{1f,h,n} We envisaged that the efficiency of the transformations might be improved by making use of the more positively charged *X*₁, causing a greater difference between the reactivities of **2** and **4**. As a metal, we were interested in Zn (EN: B = 2.0; Sn = 1.8; Zn = 1.7). We previously reported that the reaction between iodobenzenes and zinc powder smoothly takes place in *N,N,N',N'*-tetramethylurea (TMU) to afford the corresponding arylzinc compounds in good

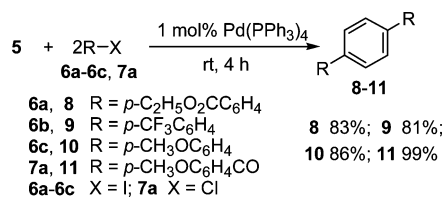
(1) See for example: *X*₁, *X*₂ = Cl, Cl: (a) Mao, L. S.; Sakurai, H.; Hirao, T. *Synthesis* **2004**, 2535–2539. *X*₁, *X*₂ = Br, Br: (b) Wu, C.-J. J.; Xue, C.; Kuo, Y.-M.; Luo, F.-T. *Tetrahedron* **2005**, 61, 4735–4741. (c) Dong, C.-G.; Hu, Q.-S. *J. Am. Chem. Soc.* **2005**, 127, 10006–10007. (d) Uozumi, Y.; Kikuchi, M. *Synlett* **2005**, 1775–1778. *X*₁, *X*₂ = I, I: (e) Sinclair, D. J.; Sherburn, M. S. *J. Org. Chem.* **2005**, 70, 3730–3733. *X*₁, *X*₂ = B, B: (f) Todd, M. H.; Balasubramanian, S.; Abell, C. *Tetrahedron Lett.* **1997**, 38, 6781–6784. (g) Bähr, A.; Felber, B.; Schneider, K.; Diederich, F. *Helv. Chim. Acta* **2000**, 83, 1346–1376. (h) Iovine, P. M.; Kellett, M. A.; Redmore, N. P.; Therien, M. J. *J. Am. Chem. Soc.* **2000**, 122, 8717–8727. (i) Chaumeil, H.; Le Drian, C.; Defoin, A. *Synthesis* **2002**, 757–760. (j) Thiemann, T.; Umeno, K.; Wang, J.; Tabuchi, Y.; Arima, K.; Watanabe, M.; Tanaka, Y.; Gorohmaru, H.; Mataka, S. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2090–2110. (k) Perret-Aebi, L.-E.; von Zelewsky, A. *Synlett* **2002**, 773–774. (l) Kalai, T.; Balog, M.; Jeko, J.; Hubbell, W. L.; Hideg, K. *Synthesis* **2002**, 2365–2372. (m) Mandolesi, S. D.; Vaillard, S. E.; Podesta, J. C.; Rossi, R. A. *Organometallics* **2002**, 21, 4886–4888. (n) Havelkova, M.; Dvorak, D.; Hockek, M. *Tetrahedron* **2002**, 58, 7431–7435. *X*₁, *X*₂ = Sn, Sn: (o) Siesel, D. A.; Staley, S. W. *J. Org. Chem.* **1993**, 58, 7870–7875. (p) Bao, Z.; Chan, W. K.; Yu, L. *J. Am. Chem. Soc.* **1995**, 117, 12426–12435. (q) Corsico, E. F.; Rossi, R. A. *Synlett* **2000**, 230–232. (r) Corsico, E. F.; Rossi, R. A. *J. Org. Chem.* **2002**, 67, 3311–3316. Reference 1m.

(2) *X*₁, *X*₂ = B, Br: (a) Shimada, S.; Yamazaki, O.; Tanaka, T.; Rao, M. L. N.; Suzuki, Y.; Tanaka, M. *Angew. Chem., Int. Ed.* **2003**, 42, 1845–1848. (b) Simoni, D.; Giannini, G.; Baraldi, P. G.; Romagnoli, R.; Roberti, M.; Rondanin, R.; Baruchello, R.; Grisolia, G.; Rossi, M.; Mirizzi, D.; Invidiata, F. P.; Grimaudo, S.; Tolomeo, M. *Tetrahedron Lett.* **2003**, 44, 3005–3008. *X*₁, *X*₂ = Zn, Br or I: (c) Amatore, C.; Jutand, A.; Negri, S.; Fauvarque, J.-F. *J. Organomet. Chem.* **1990**, 390, 389–398. (d) Krasovskiy, A.; Malakhov, V.; Gavryushin, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, 45, 6040–6044. *X*₁, *X*₂ = Li, Br: (e) Banwell, M. G.; Flynn, B. L.; Hamel, E.; Hockless, D. C. R. *Chem. Commun.* **1997**, 207–208. *X*₁, *X*₂ = Mg, Br or I: (f) Yang, X.; Rotter, T.; Piazza, C.; Knochel, P. *Org. Lett.* **2003**, 5, 1229–1231. (g) Krasovskiy, A.; Knochel, P. *Angew. Chem. Int. Ed.* **2004**, 43, 3333–3336. *X*₁, *X*₂ = Bi, Br: (h) Rasmussen, L. K.; Begtrup, M.; Ruhland, T. *J. Org. Chem.* **2006**, 71, 1230–1232.

(3) See for example: *X*₁, *X*₂ = I, Br or Cl: (a) Pena, M. A.; Perez, I.; Sestelo, J. P.; Sarandeses, L. A. *Chem. Commun.* **2002**, 2246–2247. (b) Duan, X.-F.; Li, X.-H.; Li, F.-Y.; Huang, C.-H. *Synthesis* **2004**, 2614–2616. References 1p and 2b. *X*₁, *X*₂ = OTf or I, Br or Cl (c) Ohe, T.; Miyaura, N.; Suzuki, A. *J. Org. Chem.* **1993**, 58, 2201–2208. (d) Rotländer, M.; Palmer, N.; Knochel, P. *Synlett* **1996**, 573–575. (e) Fürstner, A.; Leitner, A. *Angew. Chem., Int. Ed.* **2003**, 42, 308–311. (f) Cho, C.-H.; Kim, I.-S.; Park, K. *Tetrahedron* **2004**, 60, 4589–4599. (g) Cho, C.-H.; Park, H.; Park, M.-A.; Ryoo, T.-Y.; Lee, Y.-S.; Park, K. *Eur. J. Org. Chem.* **2005**, 3177–3181.

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SCHEME 1. Synthesis of Symmetrically 1,4-Disubstituted Benzenes



yields.⁵ In this paper, we intended to achieve the efficient synthesis of **1** with unsymmetrical structures starting from the synthetic equivalent of **3a** using the readily available Zn derivatives of **2**, $X_1 = X_2 = \text{ZnI}$, through the investigation into the effect of the phosphorus ligand affecting the discriminating ability of the Pd catalyst between the reactivities of **2** and **4**.

First, to see the utility of the zinc compound, 1,4-bis-(iodozinc)benzene **5**, in the Negishi reaction, the cross-coupling with various aryl iodides **6a–c** or aroyl chlorides **7a** (2.4 equiv) was carried out in the presence of Pd(PPh₃)₄.⁶ The obtained results, summarized in Scheme 1, show that the desired products **8–11**, symmetrically 1,4-disubstituted benzenes, were obtained in good yields under mild conditions, proving that the compound is superior to the corresponding B^{1g-n} or Sn derivatives^{1n-f} in the related Pd-catalyzed reactions, with respect to the employed conditions and/or yields.^{1h,i,n-p}

The reaction of **5** with 4-iodo(trifluoromethyl)benzene **6b** (1.0 equiv) was examined to determine if the single cross-coupling product was selectively obtained upon decreasing the amount of carbon electrophiles to one-half of the amount used in Scheme 1. After the stirring of the solution for 1 h at room temperature, the resulting solution, treated with I₂ to determine the yield of 4'-(trifluoromethyl)biphenyl-4-ylzinc iodide **12** as its derivative, 4-iodo-4'-(trifluoromethyl)biphenyl **13**, showed the presence of **12** in 69% yield along with 10% of the double coupling product **9** (entry 1 in Table 1). Although the yield of **12** might be satisfactory for practical use, a higher one is desirable, due to the difficulty in purifying the arylzinc compounds.

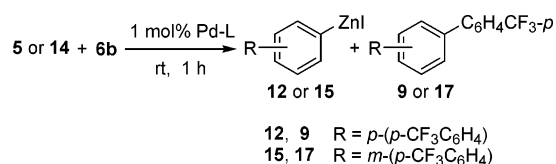
The effect of the ligands was then investigated using the palladium catalysts, generated in situ from $\text{PdCl}_2(\text{C}_6\text{H}_5\text{CN})_2$ and various phosphorus ligands possessing individual electronic and sterically demanding properties. The obtained results are summarized in Table 1 together with the electronic parameter χ^7 and steric parameter θ^8 of the ligands.

(5) (a) Takagi, K. *Chem. Lett.* **1993**, 469–472. (b) Takagi, K.; Shimoishi, Y.; Sasaki, K. *Chem. Lett.* **1994**, 2055–2088. (c) Okano, M.; Amano, M.; Takagi, K. *Tetrahedron Lett.* **1998**, 39, 3001–3004. (d) Ogawa, Y.; Saiga, A.; Mori, M.; Shibata, T.; Takagi, K. *J. Org. Chem.* **2000**, 65, 1031–1036. (e) Ikegami, R.; Koresawa, A.; Shibata, T.; Takagi, K. *J. Org. Chem.* **2003**, 68, 2195–2199.

(6) To the best of our knowledge, the direct synthesis of *p*- or *m*-phenylenedizinc compound **5** or **14** from the corresponding dihalobenzene and zinc powder has not been reported. For the direct synthesis of **5** using activated zinc, see: (a) Zhu, L.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1991**, 56, 1445–1453. For the direct synthesis of **5** or **14** using zinc powder in the presence of Co catalyst, see: (b) Kazmierski, I.; Gosmini, C.; Paris, J.-M.; Perichon, J. *Tetrahedron Lett.* **2003**, 44, 6417–6420. (c) Fillon, H.; Gosmini, C.; Perichon, J. *J. Am. Chem. Soc.* **2003**, 125, 3867–3870. (d) Fillon, H.; Gosmini, C.; Nedelec, J.-Y.; Perichon, J. *Tetrahedron Lett.* **2001**, 42, 3843–3846. For the application of **5** to the Negishi reaction, the synthesis of polymer from **5** was only reported: (e) Mellah, M.; Labbe, E.; Nedelec, J.-Y.; Perichon, J. *New J. Chem.* **2002**, 26, 207–212.

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TABLE 1. Effect of Ligand on Pd-Catalyzed Reaction of **5** or **14**^a



entry	L		yield ^b /%				property of L	
			12	15	9	17	χ^c	θ^d/deg
1 ^e	Ph ₃ P	P ₁	69		10		13.25	145
2	(<i>p</i> -CH ₃ OC ₆ H ₄) ₃ P	P ₂	64		13		10.5	145
3	(<i>p</i> -CH ₃ C ₆ H ₄) ₃ P	P ₃	60		12		11.5	145
4	Ph ₃ P		66		10		13.25	145
5	(<i>p</i> -ClC ₆ H ₄) ₃ P	P ₄	70		9		16.8	145
6	(<i>p</i> -CF ₃ C ₆ H ₄) ₃ P	P ₅	72		8		20.5	145
7	TTMOP	P ₆	49		15		−8	184
8	(<i>o</i> -CH ₃ C ₆ H ₄) ₃ P	P ₇	59		14		10.65	178
9	(C ₆ F ₅) ₃ P	P ₈	63		11		34.8	184
10	Bu ₃ P	P ₉	54		14		5.25	136
11	<i>t</i> -Bu ₃ P	P ₁₀	78		7		0	182
12 ^f	<i>t</i> -Bu ₃ P		78		5			
13 ^g	<i>t</i> -Bu ₃ P		80		6			
14 ^h	<i>t</i> -Bu ₃ P		80		8			
15	(<i>p</i> -CH ₃ C ₆ H ₄) ₃ P			46		18	11.5	145
16	Ph ₃ P			49		15	13.25	145
17	(<i>p</i> -CF ₃ C ₆ H ₄) ₃ P			59		14	20.5	145
18	<i>t</i> -Bu ₃ P			73		8	0	182

^a **5** or **14** (0.5 mmol), **6b** (0.5 mmol), PdCl₂(PhCN)₂ (0.005 mmol), L (0.02 mmol), TMU (0.3 mL), and THF (2.5 mL) were used in every run. ^b GLC yield. Yield of **12** or **15** was calculated from 4- or 3-iodo-4'-trifluoromethylbiphenyl **13** or **16**, respectively, obtained by the I₂ treatment of the reaction solutions. ^c χ = electronic parameter. ^d θ = steric parameter, cone angle. ^e Pd(PPh₃)₄ was used in place of PdCl₂(PhCN)₂. ^f Bis(dibenzylideneacetone)palladium was used in place of PdCl₂(PhCN)₂. ^g Bis[(η^3 -allyl)- μ -chloropalladium] (0.0025 mmol) was used in place of PdCl₂(PhCN)₂. ^h Bis[(η^3 -allyl)- μ -chloropalladium] (0.000025 mmol) and P(*t*-Bu)₃ (0.0002 mmol) were used.

As for a series of triarylphosphines with $\theta = 145^\circ$, the yield of **12** seemingly became higher along with the concomitant decreases in the yield of **9**, when the electron-donating property was low (entries 1–6). Eventually, based on the utility of tris-{4-(trifluoromethyl)phenyl}phosphine, a 72% yield of **12** and the selectivity between **12** and **9** of 9.0 were attained. As expected, the steric bulkiness of the ligand did not necessarily increase the yield of **12** (entries 7–9), in contrast to its beneficial effect in our previous study with the *o*-phenylenedizinc compound, in which the Pd catalyst containing the bulky tris(2-methylphenyl)phosphine or tris(2,4,6-trimethoxyphenyl)phosphine (TTMOP) afforded the highest selectivity between the single/double coupling products.⁹ Among the examined triarylphosphines, $\text{P}(\text{Bu})_3$, $\theta = 136^\circ$, gave a rather poorer result than the ordinary triarylphosphines (entry 10), presumably due to the stronger electron-donating ability, whereas $\text{P}(t\text{-Bu})_3$ attained the highest yield of **12**, 78%, and the selectivity between **12** and **9** of 11.1 (entry 11). It is noted that $\text{P}(t\text{-Bu})_3$ belongs to the phosphines that are not only the most electron-donating but also the most bulky (Scheme 2). Therefore, the observed selectivity exerted by $\text{Pd}-\text{P}(t\text{-Bu})_3$ is of interest. An equally effective catalyst was also available from $\text{P}(t\text{-Bu})_3$ and other precursors such as bis(dibenzylideneacetone)palladium or bis[(η^3 -allyl)- μ -chloropalladium] (entries 12 and 13), and the amount of the

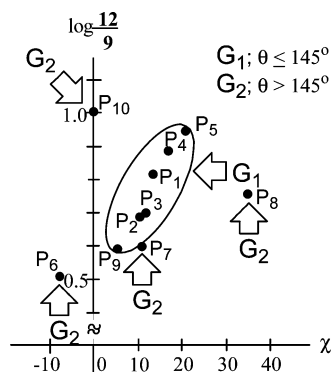
(8) Tolman, C. A. *Chem. Rev.* **1977**, 77, 313–348.

(9) Saiga, A.; Hossain, K. M.; Takagi, K. *Tetrahedron Lett.* **2000**, 41, 4629–4632.

TABLE 2. Pd–P(*t*-Bu)₃-Catalyzed Consecutive Reaction of **5** with Two Different Electrophiles^a

entry	R ¹ –X	Y–X	product	yield ^b (%)
1	<i>p</i> -CF ₃ C ₆ H ₄ –I	I–I	13	(78)
2	C ₆ H ₅ CO–Cl	I–I	18	(81)
3	C ₆ H ₅ –I	I–I	19	(70)
4	<i>p</i> -C ₂ H ₅ C ₆ H ₄ –I	I–I	20	(68)
5	<i>p</i> -CF ₃ C ₆ H ₄ –I	<i>p</i> -CH ₃ OC ₆ H ₄ –I	21	76
6	<i>p</i> -CF ₃ C ₆ H ₄ –I	<i>p</i> -C ₂ H ₅ O ₂ CC ₆ H ₄ –I	22	78
7	<i>p</i> -C ₂ H ₅ C ₆ H ₄ –I	<i>p</i> -CH ₃ COC ₆ H ₄ –I	23	56
8	<i>o</i> -C ₂ H ₅ C ₆ H ₄ –I	<i>p</i> -CH ₃ COC ₆ H ₄ –I	24	61
9	<i>o</i> -C ₂ H ₅ C ₆ H ₄ –I	<i>o</i> -CH ₃ COC ₆ H ₄ –I	25	55
10	<i>p</i> -NO ₂ C ₆ H ₄ –I	C ₆ H ₅ CH ₂ –Br	26	59
11	<i>p</i> -CF ₃ C ₆ H ₄ –I	(<i>Z</i>)-CH ₃ O ₂ CCH=CH–I	27	68
12	<i>p</i> -CF ₃ C ₆ H ₄ –I	C ₆ H ₅ CO–Cl	28	78

^a Molar ratio: 5/R–X/Y–X/Pd–*t*-Bu₃P = 1:1:1.2:0.01. In entries 1–4, I₂ was used in excess. ^b Isolated yield. Yields in parentheses determined by GLC.

SCHEME 2. Relationship between Log{(yield of **12**)/(yield of **9**)} and σ -Donicity of Ligand, χ 

catalyst was reduced to 0.01 mol % without any significant drop in the efficiency in the catalysis (entry 14).

To see if the efficiency of Pd–P(*t*-Bu)₃ is ubiquitously observed in phenylene systems, the reactions of the *m*-phenylenedizinc compound **14**⁶ with **6b** were examined. The results show that, in comparison with a series of Pd–triarylphosphines, Pd–P(*t*-Bu)₃ exhibited a far more effective catalysis, affording a 73% yield of the desired product, 4′-(trifluoromethyl)biphenyl-3-ylzinc iodide **15**, detected as 3-iodo-4′-(trifluoromethyl)biphenyl **16** via I₂ treatment, and the selectivity between **15** and the double coupling product, 4,4′-bis(trifluoromethyl)-1,1′:3′,1′′-terphenyl **17**, of 9.1 (entries 15–18). Interestingly, with respect to each ligand, the yield of a single coupling product and the selectivity were lower than the respective ones with **5** (entries 3, 4, 6, and 11).

Encouraged by the established validity of Pd–P(*t*-Bu)₃ in the reaction between **5** and **6b**, the utility of other electrophiles **6d**, **6e**, **7b** in the catalytic reaction was examined. The obtained results, summarized in Table 2, show that, similar to **6b**, the aroyl chloride was subject to the efficient catalysis by Pd–P(*t*-Bu)₃, yielding the desired product **18**, derived from the single coupling product through the second reaction with I₂, in a high yield (entry 2), and iodobenzenes, even without an electron-withdrawing substituent, also afforded the desired products **19**, **20** in good yields (entries 3, 4).

Fortunately, after the reactions of **5** with an equimolar amount of electrophiles such as **6b**, **6e**, **6g**, or **6i** were completed, Pd–

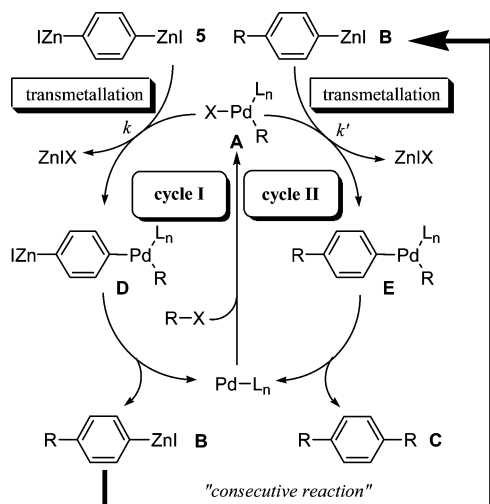
P(*t*-Bu)₃ retained the catalytic activity. Thus, the subsequent additions of other carbon electrophiles such as **6a**, **6c**, **6f**, **6h**, **6j**, **6k**, or **7b** (1.2 equiv) to the resulting solutions readily caused their catalytic cross-coupling with the incipient products to take place. The results summarized in Table 2 show that a wide variety of unsymmetrically 1,4-disubstituted benzenes, containing 4-CF₃-, 4-NO₂-, 4-C₂H₅-, or 2-C₂H₅-substituted phenyl group as the first introduced substituent and 4-C₂H₅OCO-, 4-CH₃CO-, 4-CH₃O-, or 2-CH₃CO-substituted phenyl, alkenyl, benzyl, or aroyl groups as the second introduced substituent, was obtained in good yield (entries 5–12). Thus, based on the utility of **5** and the specific catalysis by Pd–P(*t*-Bu)₃, the novel and efficient one-pot synthesis of unsymmetrically 1,4-disubstituted benzenes from the *p*-phenylenedimetallic compound was achieved.

Finally, it might be worthy to consider the reason for the high chemoselectivity achieved by Pd–P(*t*-Bu)₃, because the results are concerned with the transmetalation reaction involved in the catalytic cycle (vide infra), of which there is limited mechanistic information.¹⁰ In Scheme 3, prepared by application of the general catalytic cycle of the Negishi reaction to the present one, the double coupling product **C**, like **9**, is formed from the single coupling product **B**, like **12**, through **cycle II**, wherein exists a competition for the oxidative adduct **A** between **B** and **5**, the latter of which belongs to **cycle I** yielding **B**. During the competitive transmetalation, among the various examined Pd–L (Table 1), Pd–P(*t*-Bu)₃ significantly discriminated the difference in the reactivity between **5** and **B**, resulting in producing **B** with the highest yield.¹¹ Each of the ligands L conferred an individual catalytic efficiency on **A**, depending on its electronic property and/or steric bulkiness; however, P(*t*-Bu)₃ seems to deviate from the standard effect. That is, as shown

(10) For a general catalytic cycle of Pd-catalyzed cross-coupling including the Negishi reaction, see for example: (a) Tamao, K.; Miyaura, N. In *Cross-Coupling Reactions*; Miyaura, N., Ed.; Springer: Berlin, 2002; pp 4–7. For a transmetalation of arylpalladium complexes, see for example: (b) Suzuki, Y.; Yagyu, T.; Osakada, K. *J. Organomet. Chem.* **2007**, 692, 326–342. (c) Espinet, P.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, 43, 4704–4734. (d) Casares, J. A.; Espinet, P.; Fuentes, B.; Salas, G. *J. Am. Chem. Soc.* **2007**, 129, 3508–3509.

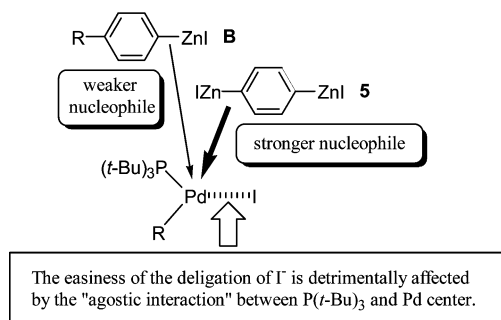
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SCHEME 3. Catalytic Cycle



in Scheme 2, for both $G_1 \theta \leq 145^\circ$ and $G_2 \theta > 145^\circ$, forming **A** of ArPdXL_2 and of ArPdXL , respectively,¹² the selectivity tended to increase as the electron-donating ability of **L** decreased, although the degrees of the increase in G_1 and of G_2 were not the same, with the exception of $\text{P}(t\text{-Bu})_3$. As the special effect by $\text{P}(t\text{-Bu})_3$, the agostic interaction in $\text{ArPdI}(\text{P}(t\text{-Bu})_3)$ brings about the noted strengthening of the bond between Pd and I.^{13,14} Such a strong Pd–I probably made the replacement of **I** with the weaker nucleophile **B** much more difficult, which might be the origin of the high chemoselectivity¹⁵ (Scheme 4). As for G_1 or G_2 , **A** containing the weakly electron-donating **L** should possess a strong corresponding bond, obeying the trans influence rule. This fact might support the hypothesis.

In conclusion, $\text{Pd}-\text{P}(t\text{-Bu})_3$ catalyst achieved the *chemoselective* cross-couplings of *p*-phenylenedizinc compounds with

SCHEME 4. Discrimination of Reactivity between **5** and **B**

an equimolar amount of aryl or aroyl electrophiles to afford the single coupling products in high yields,¹⁷ which allowed the novel and efficient access to unsymmetrically 1,4-disubstituted benzenes through the one-pot procedure.

Experimental Section

General Procedure for the Palladium-Catalyzed Consecutive Cross-Coupling of Phenylenedizinc Compound **5 with Two Kinds of Carbon Electrophiles. Preparation of 4-Methoxy-4'-trifluoromethyl-1,1':4',1''-terphenyl **21**.** To $\text{PdCl}_2(\text{PhCN})_2$ (1.9 mg, 0.005 mmol) was added THF (0.1 mL) and 0.059 mL of a hexane solution of $\text{P}(t\text{-Bu})_3$ (0.020 mmol), then the mixture was stirred for 5 min at room temperature. To the mixture was next added a 2.8 mL of THF/TMU solution of **5** (0.50 mmol) and 4-iodobenzotrifluoride **6b** (0.090 mL, 0.50 mmol); the mixture was stirred for 1 h at room temperature. To the resulting mixture, *p*-iodoanisole **6c** (131 mg, 0.60 mmol) was added and stirred for 3 h at room temperature. After the treatment of the resulting mixture with aqueous HCl, the CHCl_3 extract was thin layer chromatographed on silica gel affording 125 mg of **21** (76%): mp $196-197^\circ\text{C}$; IR (KBr) 1259 cm^{-1} , 1336 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 3.87 (s, 3H), 7.01 (d, $J = 8.8\text{ Hz}$, 2H), 7.59 (d, $J = 8.9\text{ Hz}$, 2H), 7.67–7.73 (m, 8H); ^{13}C NMR (126 MHz, $\text{CDCl}_3/\text{C}_2\text{H}_2\text{Cl}_4$) δ 55.3, 114.3, 124.2 (q, $J = 272.1\text{ Hz}$), 125.6 (q, $J = 3.9\text{ Hz}$), 127.1, 127.5, 128.0, 129.1 (q, $J = 32.5\text{ Hz}$), 132.7, 137.8, 140.5, 144.1, 159.3; Anal. Calcd for $\text{C}_{20}\text{H}_{15}\text{F}_3\text{O}$: C, 73.16; H, 4.60. Found: C, 73.10; H, 5.00.

Supporting Information Available: General method, relationship between $\log([\text{B}]/[\text{C}])$ and $\log k/k'$, the bond distance between Pd and I in ArPdI complexes, compound characterization data. This material is available free of charge via Internet at <http://pubs.acs.org>.

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(14) The bond distance between Pd and I in the complex, 2.613 Å, is one of the shortest among the various ArPdI complexes containing the phosphorus ligand. See the SI, for the details.

(15) We measured the ^{19}F NMR of *p*-fluorophenylzinc compound to determine the field/inductive parameter σ of *p*-ZnI group.¹⁶ The observed σ constant for *p*-ZnI, -0.32 , was smaller than the values reported for *p*- C_6H_5 , 0.01 , and *p*- $\text{C}_6\text{H}_5\text{CO}$, 0.41 , which means that **5** possesses a stronger nucleophilicity than the single coupling product **B**. A similar run with the *m* derivative showed that *m*-ZnI, σ constant -0.29 , also possesses a stronger electron-donating ability than *m*- C_6H_5 , 0.06 , or *m*- $\text{C}_6\text{H}_5\text{CO}$, 0.32 .

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