JOC *Note*

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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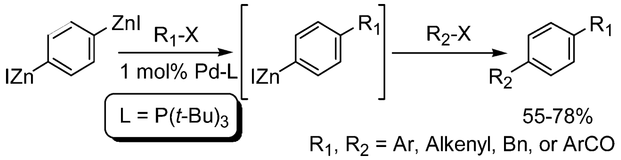

Pd−P(*t*-Bu)$_3$ was found to be a *chemoselective* catalyst for the reaction of *p*-phenylenedizinc compound with equimolar amounts of carbon electrophiles to afford the single cross-coupling products in good yields, effectively suppressing the formation of double cross-coupling products. The subsequent 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 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 Sn[2]) or **3c** (possessing $X_1 = I$ and $X_2 =$ Br or OTf[3]) 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

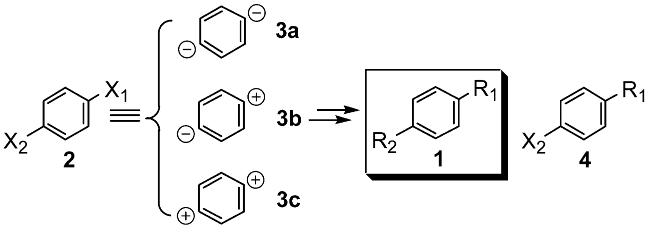

FIGURE 1. Synthesis of *p*-disubstituted benzenes.

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(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.; Hocek, 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) Rottländer, 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.

(4) X_1, X_2 = Si, Sn: (a) Nitschke, J. R.; Zürcher, S.; Tilley, T. D. *J. Am. Chem. Soc.* **2000**, *122*, 10345−10352. X_1, X_2 = Mg, B prepared successively: (b) Christophersen, C.; Begtrup, M.; Ebdrup, S.; Petersen, H.; Vedso, P. *J. Org. Chem.* **2003**, *68*, 9513−9516. X_1, X_2 = Mn, Mn prepared successively: (c) Rieke, R. D.; Kim, S.-H.; Wu, X. *J. Org. Chem.* **1997**, *62*, 6921−6927. X_1, X_2 = Mg, Mg prepared successively: ref 2f.

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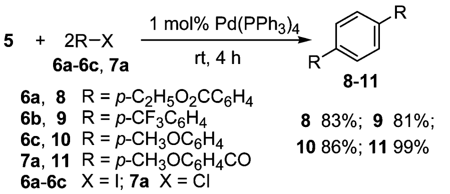
SCHEME 1. Synthesis of Symmetrically 1,4-Disubstituted Benzenes



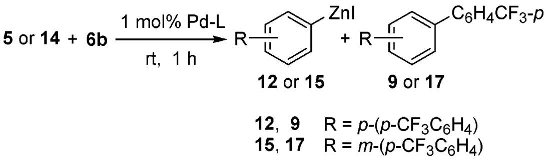
yields.[5] In this paper, we intended to achieve the efficient synthesis of **1** with unsymmetrical structures starting from the synthetic equivalent of **3a** using the readily available Zn derivatives of **2**, $X_1 = X_2 = \mathrm{ZnI}$, through the investigation into the effect of the phosphorus 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 $Pd(PPh_3)_4$.[6] The obtained results, summarized in Scheme 1, show that the desired products **8−11**, symmetrically 1,4-disubstututed 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−r] 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 I_2 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 $PdCl_2(C_6H_5CN)_2$ 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.

TABLE 1. Effect of Ligand on Pd-Catalyzed Reaction of 5 or 14[a]



			yield[b]/%				property of L	
entry	L		**12**	**15**	**9**	**17**	χ[c]	θ[d]/deg
1[e]	Ph_3P	P_1	69		10		13.25	145
2	$(p\text{-}CH_3OC_6H_4)_3P$	P_2	64		13		10.5	145
3	$(p\text{-}CH_3C_6H_4)_3P$	P_3	60		12		11.5	145
4	Ph_3P		66		10		13.25	145
5	$(p\text{-}ClC_6H_4)_3P$	P_4	70		9		16.8	145
6	$(p\text{-}CF_3C_6H_4)_3P$	P_5	72		8		20.5	145
7	TTMOP	P_6	49		15		−8	184
8	$(o\text{-}CH_3C_6H_4)_3P$	P_7	59		14		10.65	178
9	$(C_6F_5)_3P$	P_8	63		11		34.8	184
10	Bu_3P	P_9	54		14		5.25	136
11	$t\text{-}Bu_3P$	P_{10}	78		7		0	182
12[f]	$t\text{-}Bu_3P$		78		5			
13[g]	$t\text{-}Bu_3P$		80		6			
14[h]	$t\text{-}Bu_3P$		80		8			
15	$(p\text{-}CH_3C_6H_4)_3P$			46		18	11.5	145
16	Ph_3P			49		15	13.25	145
17	$(p\text{-}CF_3C_6H_4)_3P$			59		14	20.5	145
18	$t\text{-}Bu_3P$			73		8	0	182

[a] **5** or **14** (0.5 mmol), **6b** (0.5 mmol), $PdCl_2(PhCN)_2$ (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 I_2 treatment of the reaction solutions. [c] χ = electronic parameter. [d] θ = steric parameter, cone angle. [e] $Pd(PPh_3)_4$ was used in place of $PdCl_2(PhCN)_2$. [f] Bis(dibenzylideneacetone)palladium was used in place of $PdCl_2(PhCN)_2$. [g] Bis[(η^3-allyl)-μ-chloropalladium] (0.0025 mmol) was used in place of $PdCl_2(PhCN)_2$. [h] Bis[(η^3-allyl)-μ-chloropalladium] (0.000025 mmol) and $P(t\text{-}Bu)_3$ (0.0002 mmol) were used.

As for a series of triarylphosphines with $\theta = 145°$, 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 trialkylphosphines, $P(Bu)_3$, $\theta = 136°$, gave a rather poorer result than the ordinary triarylphosphines (entry 10), presumably due to the stronger electron-donating ability, whereas $P(t\text{-}Bu)_3$ attained the highest yield of **12**, 78%, and the selectivity between **12** and **9** of 11.1 (entry 11). It is noted that $P(t\text{-}Bu)_3$ 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 Pd−$P(t\text{-}Bu)_3$ is of interest. An equally effective catalyst was also available from $P(t\text{-}Bu)_3$ and other precursors such as bis(dibenzylideneacetone)palladium or bis[(η^3-allyl)-μ-chloropalladium] (entries 12 and 13), and the amount of the

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[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.

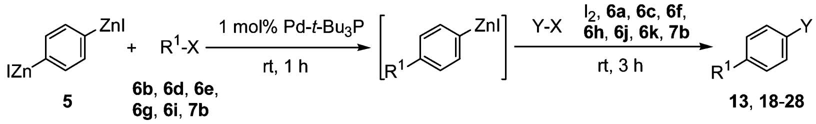
[6] To the best of our knowledge, the direct synthesis of *p*- or *m*-phenylenedizinc compound **5** or **14** from the corresponding dihalobenzene and zinc powder has not been reported. For the direct synthesis of **5** using activated zinc, see: (a) Zhu, L.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **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.

[7] (a) Bartik, T.; Himmler, T.; Schulte, H. G.; Seevogel, K. *J. Organomet. Chem.* **1984**, *272*, 29−41. (b) Liu, H. Y.; Eriks, K.; Prock, A.; Giering, W. P. *Organometallics* **1990**, *9*, 1758−1766.

[8] Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313−348.

[9] Saiga, A.; Hossain, K. M.; Takagi, K. *Tetrahedron Lett.* **2000**, *41*, 4629−4632.

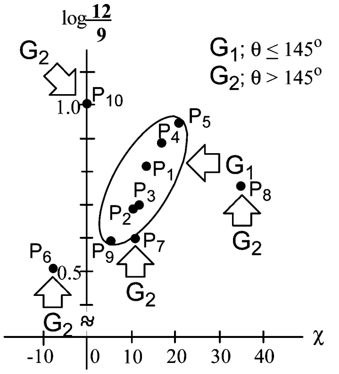
TABLE 2. **Pt−P(t-Bu)$_3$-Catalyzed Consecutive Reaction of 5 with Two Different Electrophiles**[a]



entry	R^1−X		Y−X		product	yield[b] (%)
1	*p*-$CF_3C_6H_4$−I	**6b**	I−I		**13**	(78)
2	C_6H_5CO−Cl	**7b**	I−I		**18**	(81)
3	C_6H_5−I	**6d**	I−I		**19**	(70)
4	*p*-$C_2H_5C_6H_4$−I	**6e**	I−I		**20**	(68)
5	*p*-$CF_3C_6H_4$−I	**6b**	*p*-$CH_3OC_6H_4$−I	**6c**	**21**	76
6	*p*-$CF_3C_6H_4$−I	**6b**	*p*-$C_2H_5O_2CC_6H_4$−I	**6a**	**22**	78
7	*p*-$C_2H_5C_6H_4$−I	**6e**	*p*-$CH_3COC_6H_4$−I	**6f**	**23**	56
8	*o*-$C_2H_5C_6H_4$−I	**6g**	*p*-$CH_3COC_6H_4$−I	**6f**	**24**	61
9	*o*-$C_2H_5C_6H_4$−I	**6g**	*o*-$CH_3COC_6H_4$−I	**6h**	**25**	55
10	*p*-$NO_2C_6H_4$−I	**6i**	$C_6H_5CH_2$−Br	**6j**	**26**	59
11	*p*-$CF_3C_6H_4$-I	**6b**	(*Z*)-CH_3O_2CCH═CH−I	**6k**	**27**	68
12	*p*-$CF_3C_6H_4$−I	**6b**	C_6H_5CO−Cl	**7b**	**28**	78

[a] Molar ratio: **5**/R−X/Y−X/Pd−*t*-Bu$_3$P = 1:1:1.2:0.01. In entries 1−4, I_2 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)bipenyl **16** via I_2 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 I_2, 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-CF_3-, 4-NO_2-, 4-C_2H_5-, or 2-C_2H_5-substituted phenyl group as the first introduced substituent and 4-C_2H_5OCO-, 4-CH_3CO-, 4-CH_3O-, or 2-CH_3CO-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 unsymmetrically1,4-disubstituted benzenes from the *p*-phenylenedimetallic compound was achieved.

Finally, it might be worthy to consider the reason for the high chemoslectivity achieved by Pd−P(*t*-Bu)$_3$, because the results are concerned with the transmetallation 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 transmetallation, 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

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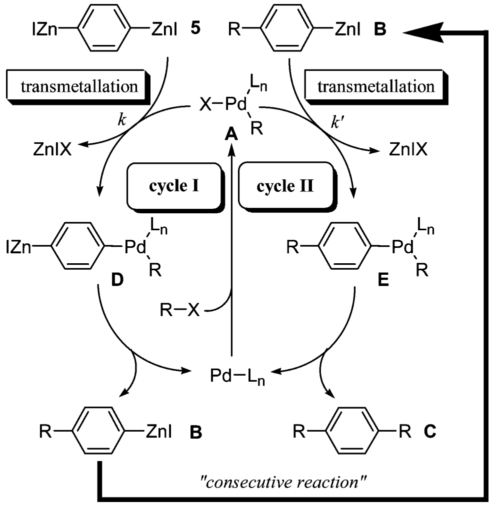
[10] For a general catalytic cycle of Pd-catalyzed cross-coupling including the Negishi reaction, see for example: (a) Tamao, K.; Miyaura, N. In *Cross-Coupling Reactions*; Miyaura, N., Ed.; Springler: Berlin, 2002; pp 4−7. For a transmetallation of arylpalladium complexes, see for example: (b) Suzaki, 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.

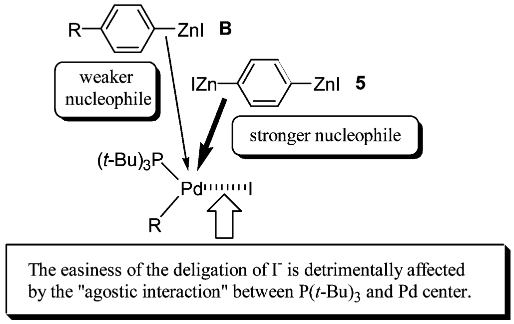
[11] (a) Negishi, E.; Takahashi, T.; Baba, S.; Van Horn, D. E.; Okukado, N. *J. Am. Chem. Soc.* **1987**, *109*, 2393−2401. (b) Amatore, C.; Jutand, A. In *Handbook of Organopalladium Chemistry*; Negishi, E., Ed.; John Wiley & Sons: New York 2002; pp 943−965. See the Supporting Information (SI) for the details.

SCHEME 3. Catalytic Cycle



in Scheme 2, for both G_1 $\theta \leq 145°$ and G_2 $\theta > 145°$, 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 P(*t*-Bu)$_3$. As the special effect by P(*t*-Bu)$_3$, the agostic interaction in ArPdI(P(*t*-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 chemoselectivity[15] (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.

SCHEME 4. Discrimination of Reactivity between 5 and B



In conclusion, Pd−P(*t*-Bu)$_3$ catalyst achieved the *chemoselective* cross-couplings of *p*-phenylenedizinc compounds with 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-Couplng of Phenylenedizinc Compound 5 with Two Kinds of Carbon Electrophiles. Preparation of 4-Methoxy-4″-trifluoromethyl-1,1′:4′,1″-terphenyl 21. To $PdCl_2(PhCN)_2$ (1.9 mg, 0.005 mmol) was added THF (0.1 mL) and 0.059 mL of a hexane solution of P(*t*-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 °C; IR (KBr) 1259 cm^{-1}, 1336 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.87 (s, 3H), 7.01 (d, $J = 8.8$ Hz, 2H), 7.59 (d, $J = 8.9$ Hz, 2H), 7.67−7.73 (m, 8H); ^{13}C NMR (126 MHz, $CDCl_3/C_2H_2Cl_4$) δ 55.3, 114.3, 124.2 (q, $J = 272.1$ Hz), 125.6 (q, $J = 3.9$ Hz), 127.1, 127.5, 128.0, 129.1 (q, $J = 32.5$ Hz), 132.7, 137.8, 140.5, 144.1, 159.3; Anal. Calcd for $C_{20}H_{15}F_3O$: C, 73.16; H, 4.60. Found: C, 73.10; H, 5.00.

Supporting Information Available: General method, relationship between log([**B**]/[**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, 2.613A, 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 $c\sigma$ of *p*-ZnI group.[16] The observed $c\sigma$ constant for *p*-ZnI, −0.32, was smaller than the values reported for *p*-C_6H_5, 0.01, and *p*-C_6H_5CO, 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, $c\sigma$ constant −0.29, also possesses a stronger electron-donating ability than *m*-C_6H_5, 0.06, or *m*-C_6H_5CO, 0.32.

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(17) Pd−P(*t*-Bu)$_3$ affords the double coupling products selectively in the reaction of dihalobenzenes with equimolar amounts of arylboronic acids: Reference 1e. See also: Yokoyama, A.; Suzuki, H.; Kubota, Y.; Ohuchi, K.; Higashimura, H.; Yokozawa, T. *J. Am. Chem. Soc.* **2007**, *129*, 7236−7237.