JOC Note

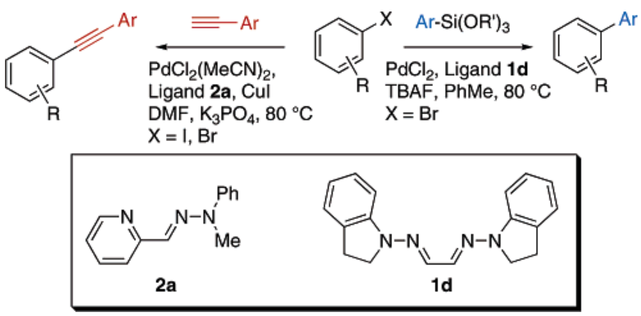
Palladium-Catalyzed Sonogashira and Hiyama Reactions Using Phosphine-Free Hydrazone Ligands

Takashi Mino,* Yoshiaki Shirae, Takeshi Saito, Masami Sakamoto, and Tsutomu Fujita

Department of Applied Chemistry and Biotechnology, Faculty of Engineering, Chiba University, 1-33, Yayoi-cho, Inage-ku, Chiba 263-8522, Japan

tmino@faculty.chiba-u.jp

Received August 21, 2006



Palladium/copper-catalyzed Sonogashira cross-coupling reaction of aryl halides with a variety of terminal alkynes under amine-free conditions in dimethylformamide (DMF) at 80 °C gave internal arylated alkynes using $PdCl_2(MeCN)_2$ with phosphine-free hydrazone **2a** as a ligand and CuI as the cocatalyst in good yields. We also found $PdCl_2$/hydrazone ligand **1d** in PhMe at 80 °C was a phosphine-free efficient catalyst system for a Hiyama cross-coupling reaction of aryl bromides with aryl(trialkoxy)silanes in good yields.

Palladium-catalyzed C−C coupling reactions have been recognized as powerful tools in multiple organic transformations.[1] We recently demonstrated air-stable phosphine-free hydrazone as an effective ligand for the Suzuki−Miyaura[2] and Mizoroki−Heck cross-coupling reaction.[3]

The Sonogashira cross-coupling reaction of aryl halides with terminal acetylenes, which provides a powerful tool for the formation of alkynes, has been widely applied to such diverse areas as natural product syntheses and material science.[4] The most common catalytic system for this reaction is using such palladium−phosphine complexes as $PdCl_2(PPh_3)_2$ and $Pd(PPh_3)_4$ in large amounts of amines as solvents or cosolvents with CuI as the cocatalyst.[5−7] Recently a copper-free Sonogashira cross-coupling reaction was reported that used a combination of at least one phosphine as a ligand or an amine and a large amount of tetra-*n*-butyl ammonium salt as an activator.[8−10] However, their phosphines in palladium complexes are often air-sensitive. Amines also have a characteristic foul smell and pungent flavor. We now report the use of air-stable phosphine-free hydrazone ligands **1** and **2** for an amine-free palladium/copper-catalyzed Sonogashira cross-coupling reaction.

We applied the coupling of 4-iodotoluene and phenyl acetylene in the presence of 2 mol % of $PdCl_2(MeCN)_2$ with K_3PO_4 as a base under an argon atmosphere at 80 °C to determine the optimum reaction conditions (Table 1). The effect of various hydrazone ligands in this reaction was investigated (entries 1−5). In the presence of glyoxal bis(*N*-methyl-*N*-phenylhydrazone) (**1a**), which was the effective ligand for the

(1) For reviews, see the following: (a) Larhed, M.; Hallberg, A. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley-Interscience: New York, 2002; Vol. 1, p 1133. (b) Whitcombe, N. J.; Hii, K. K.; Gibson, S. E. *Tetrahedron* **2001**, *57*, 7449. (c) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009. (d) Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules*, 2nd ed.; University Science Books: Sausalito, CA, 1999; Chapter 4.6. (e) Brase, S.; de Meijere, A. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998; Chapter 3. (f) Link, J. T.; Overman, L. E. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998; Chapter 6. (g) Beller, M.; Riermeier, T. H.; Stark, G. In *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, Germany, 1998; Vol. 1, p 208. (h) Crisp, G. T. *Chem. Soc. Rev.* **1998**, *27*, 427. (i) Tsuji, J. *Palladium Reagents and Catalysts: Innovations in Organic Synthesis*; Wiley: Chichester, U.K., 1995.

(2) (a) Mino, T.; Shirae, Y.; Sakamoto, M.; Fujita, T. *Synlett* **2003**, 882. (b) Mino, T.; Shirae, Y.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2005**, *70*, 2191.

(3) Mino, T.; Shirae, Y.; Sasai, Y.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2006**, *71*, 6837.

(4) For reviews, see the following: (a) Sonogashira, K. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998; Chapter 5. (b) Brandsma, L.; Vasilevsky, S. F.; Verkruijsse, H. D. *Application of Transition Metal Catalysts in Organic Synthesis*; Springer-Verlag: Berlin, 1998; Chapter 10. (c) Sonogashira, K. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: New York, 1991; Vol. 3, Chapter 2.4.

(5) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *44*, 4467. (b) Cassar, L. *J. Organomet. Chem.* **1975**, *93*, 253. (c) Dieck, H. A. Heck, R. F. *J. Organomet. Chem.* **1975**, *93*, 259.

(6) For examples, see the following: (a) Thorand, S.; Krause, N. *J. Org. Chem.* **1998**, *63*, 8551. (b) Hundertmark, T.; Litter, A. F.; Buchwald, S. L.; Fu, G. C. *Org. Lett.* **2000**, *2*, 1729. (c) Chow, H.-F.; Wan, C.-W.; Low, K.-H.; Yeung, Y.-Y. *J. Org. Chem.* **2001**, *66*, 1910. (d) Novák, Z.; Szabó, A.; Répási, J.; Kotschy, A. *J. Org. Chem.* **2003**, *68*, 3327. (e) Remmele, H.; Köllhofer, A.; Plenio, H. *Organometallics* **2003**, *22*, 4098. (f) Elangovan, A.; Wang, Y.-H.; Ho, T.-I. *Org. Lett.* **2003**, *5*, 1841. (g) Adjabeng, G.; Brenstrum, T.; Frampton, C. S.; Robertson, A. J.; Hillhous, J.; McNulty, J.; Capretta, A. *J. Org. Chem.* **2004**, *69*, 5082. (h) Son, S. U.; Jang, Y.; Park, J.; Na, H. B.; Park, H. M.; Yun, H. J.; Lee, J.; Hyeon, T. *J. Am. Chem. Soc.* **2004**, *126*, 5026. (i) Hierso, J.-C.; Fihri, A.; Amardeil, R.; Meunier, P. *Org. Lett.* **2004**, *6*, 3473.

(7) Recently copper-catalyzed Sonogashira cross-coupling reaction under palladium and phosphine-free conditions was reported: Ma, D.; Liu, F. *Chem. Commun.* **2004**, 1934.

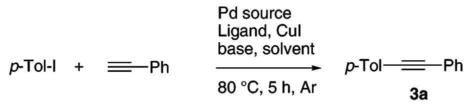
(8) For a selected paper on the copper-free conditions using phosphine/amine, see the following: Soheili, A.; Albaneze-Walker, J.; Murry, J. A.; Dormer, P. G.; Hughes, D. L. *Org. Lett.* **2003**, *5*, 4191.

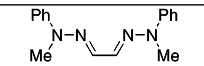
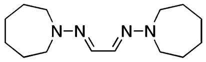
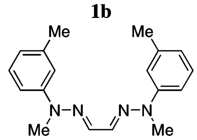
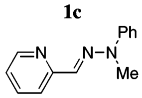
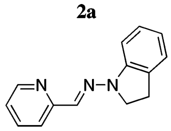
(9) For selected papers on the copper and amine-free conditions using phosphine, see the following: (a) Cheng, J.; Sun, Y.; Wang, F.; Guo, M.; Xu, J.-H.; Pan, Y.; Zhang, Z. *J. Org. Chem.* **2004**, *69*, 5428. (b) Liang, Y.; Xie, Y.-X.; Li, J.-H. *J. Org. Chem.* **2006**, *71*, 379. (c) Yi, C.; Hua, R. *J. Org. Chem.* **2006**, *71*, 2535.

(10) For selected papers on the copper and phosphine-free conditions using amine or tetra-*n*-butyl ammonium salt, see: (a) Park, S. B.; Alper, H. *Chem. Commun.* **2004**, 1306. (b) Urgaonkar, S.; Verkade, J. G. *J. Org. Chem.* **2004**, *69*, 5752. (c) Liang, B.; Dai, M.; Chen, J.; Yang, Z. *J. Org. Chem.* **2005**, *70*, 391.

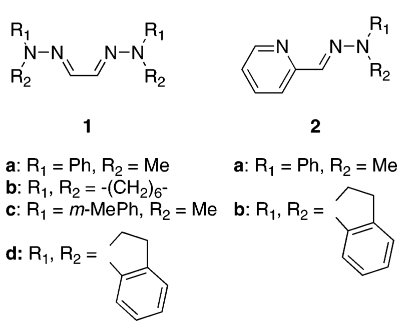
10.1021/jo061734i CCC: $33.50
Published on Web 11/08/2006

TABLE 1. Optimization of Reaction Conditions on Sonogashira Reaction[a]



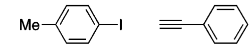
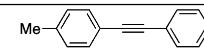
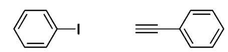
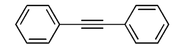
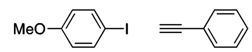
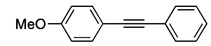
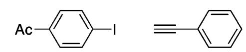
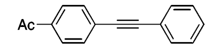
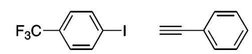
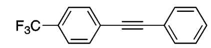
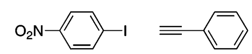
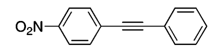
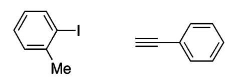
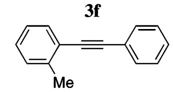
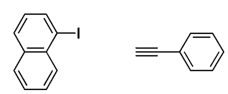
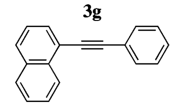
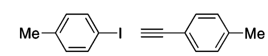
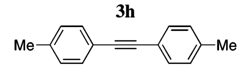
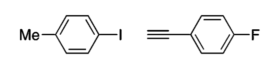
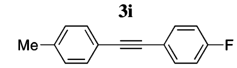
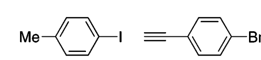
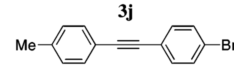
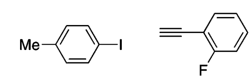
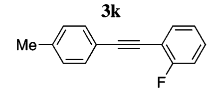
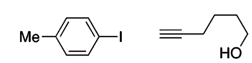
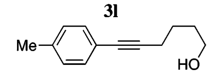
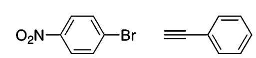
entry	ligand	base	solvent	Pd source	yield (%)[b]
1	 **1a**	K_3PO_4	DMF	$PdCl_2(MeCN)_2$	75
2	 **1b**	K_3PO_4	DMF	$PdCl_2(MeCN)_2$	37
3	 **1c**	K_3PO_4	DMF	$PdCl_2(MeCN)_2$	46
4	 **2a**	$\mathbf{K_3PO_4}$	**DMF**	$\mathbf{PdCl_2(MeCN)_2}$	**93**
5	 **2b**	K_3PO_4	DMF	$PdCl_2(MeCN)_2$	27
6	–	K_3PO_4	DMF	$PdCl_2(MeCN)_2$	41
7	**2a**	Cs_2CO_3	DMF	$PdCl_2(MeCN)_2$	76
8	**2a**	K_2CO_3	DMF	$PdCl_2(MeCN)_2$	37
9	**2a**	NaOAc	DMF	$PdCl_2(MeCN)_2$	17
10	**2a**	KO^{t}Bu	DMF	$PdCl_2(MeCN)_2$	9
11	**2a**	K_3PO_4	PhMe	$PdCl_2(MeCN)_2$	4
12	**2a**	K_3PO_4	MeCN	$PdCl_2(MeCN)_2$	70
13	**2a**	K_3PO_4	NMP	$PdCl_2(MeCN)_2$	59
14	**2a**	K_3PO_4	DMF	$Pd(OAc)_2$	88
15	**2a**	K_3PO_4	DMF	$PdCl_2$	74
16	**2a**	K_3PO_4	DMF	$Pd_2(dba)_3{\cdot}CH_3Cl$	83

[a] Reaction conditions: 4-iodotoluene (1 mmol), phenyl acetylene (1.2 mmol), base (1.4 mmol), solvent (2 mL), palladium source (0.02 mmol), ligand (0.02 mmol), CuI (0.05 mmol). [b] Isolated yields.



Suzuki−Miyaura reaction, Sonogashira cross-coupling product **3a** was obtained in moderate yield (entry 1). Bishydrazone ligand **1b** with a seven-membered ring was not effective for this reaction. The use of **2a** as a ligand led to high yield for this reaction (entry 4). Without the presence of ligand **2a**, the reaction gave low yield of the desired product (entry 4 vs entry 6). The effect of various bases in the Sonogashira cross-coupling reaction was investigated (entries 4, 7−10). Among inorganic bases (K_3PO_4, Cs_2CO_3, and K_2CO_3), NaOAc, and KO^{t}Bu examined in DMF (*N*,*N*-dimethylformamide), K_3PO_4 proved very effective. Other solvents proved less effective in this reaction than DMF (entry 4 vs entries 11−13). Several commonly used palladium sources were also tested (entries 4, 14−16); $PdCl_2(MeCN)_2$ preferred this reaction (entry 4).

TABLE 2. Sonogashira Reaction of Aryl Halides with Alkynes[a]

entry	aryl halide / alkyne	time (h)	product	yield (%)[b]
1		5	 **3a**	93
2		5	 **3b**	94
3		5	 **3c**	87
4		5	 **3d**	74
5		5	 **3e**	81
6		5	 **3f**	84
7		5	 **3g**	83
8[c]		5	 **3h**	95
9		5	 **3i**	83
10[c]		5	 **3j**	70
11[c]		5	 **3k**	48
12[c]		5	 **3l**	95
13[c,d]		5	 **3m**	73
14[e]		24	**3f**	51

[a] Reaction conditions: aryl halide (1 mmol), alkyne (1.2 mmol), K_3PO_4 (1.4 mmol), DMF (2 mL), PdCl2(MeCN)2 (0.02 mmol), ligand 2a (0.02 mmol), CuI (0.05 mmol). [b] Isolated yields. [c] 4-Iodotoluene (0.5 mmol) and alkyne (1.0 mmol) were added. [d] This reaction was carried out at 70 °C. [e] This reaction used 2 equiv of phenyl acetylene.

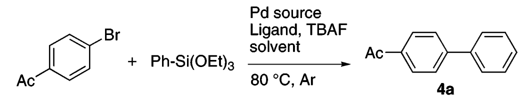
The effect of various aryl iodides in the Sonogashira cross-coupling reaction was investigated using phenyl acetylene (entries 1−8, Table 2). Using 4-substituted aryl iodides led to good yields of the desired products (entries 1−6). Moreover, 2-substituted aryl iodides also led to good yields (entry 7). Using a 4 mol % palladium catalyst, the reaction of 1-iodonaphthalene with phenyl acetylene gave corresponding product with good yield (entry 8). The effect of varying alkynes was also investigated using 4-iodotoluene as the substrate (entries 9−13). Using 4-ethynyltoluene led to good yield of the corresponding product (entry 9). The reaction of 4-bromo-1-nitorobenzene with phenyl acetylene was necessary for longer reaction times such as 24 h (entry 14).

We next tried Hiyama cross-coupling of aryl bromides with aryl(trialkoxy)silanes using air-stable phosphine-free hydrazones **1** and **2** as a ligand. This reaction also provides a powerful tool for the C−C bond formation of biaryls, which has been widely applied to such diverse areas as natural product and biologically active compound synthesis.[11] The use of such silicon-derived compounds as transmetalation reagents has attracted much attention as a viable option to these processes for its low cost, easy availability, nontoxic byproducts, and stability under many reaction conditions.[12] Generally, the Hiyama cross-coupling reaction is also carried out using an air-sensitive phosphine–palladium catalyst such as $Pd(OAc)_2/PPh_3$ and $PdCl_2(MeCN)_2/(o\text{-Tol})_3P$.[12f,l] We now report the use of air-stable hydrazone ligands **1** and **2** for phosphine-free palladium-catalyzed Hiyama cross-coupling reactions. We optimized the coupling conditions of 4-bromoacetophenone with phenyl(triethoxy)silane at 80 °C (Table 3). The effect of ligands in this reaction was investigated (entries 1–5). In the presence of **1d**, cross-coupling product **4a** was obtained in good yield (entry 3). Pyridine-type hydrazone ligands **2a** and **2b** were ineffective for this reaction. The effect of various solvents was investigated using ligand **1d** (entries 3, 6–10). Toluene proved very effective for 5 h (entry 10). Other solvents proved less effective in this reaction. Without the presence of ligand **1d**, the yield was decreased (entry 10 vs entry 11). Several commonly used palladium sources were also tested (entries 4, 12–14). We found the following optimized conditions: using the $PdCl_2$/hydrazone **1d** system, the reaction proceeded with 83% in toluene at 80 °C under an argon atmosphere (entry 14).

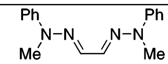
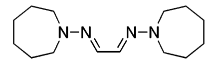
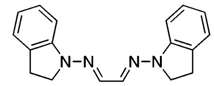
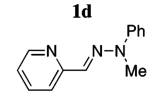
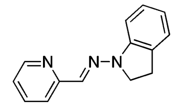
On the basis of those results, the Hiyama reaction of aryl bromides with various siloxanes was investigated (Table 4). The reaction of 4-bromoacetophenone and phenyl(triethoxy)silane gave corresponding product with 73% yield for 3 h (entry 2). Using phenyl(trimethoxy)silane, instead of phenyl(triethoxy)-silane, also led to good yield (entry 3). Although a 4-methoxyphenyl bromide led to low yield (entry 6), the reactions of other 4-substituted aryl bromides gave good yields of the corresponding products (entries 5, 7, and 8). Moreover, 3-substituted aryl bromides and 1-bromonaphthalene also led to good yields (entries 9–11). We also investigated the reaction of 2-substituted aryl bromides. Using 3 equiv of phenyl(triethoxy)-silane led to moderate yields of the corresponding products (entries 12 and 13). The reaction of bromobenzene with various aryl(triethoxy)silanes gave corresponding products with moderate to good yields (entries 14–17).

We found that hydrazone **2a** was useful as a phosphine-free ligand for the palladium/copper-catalyzed Sonogashira cross-coupling reaction of aryl halides with a variety of terminal alkynes under amine-free conditions in DMF at 80 °C with $PdCl_2(MeCN)_2$. We also found that $Pd(OAc)_2$/hydrazone ligand **1d** in PhMe at 80 °C was a phosphine-free efficient catalyst system for Hiyama cross-coupling reaction of aryl bromides with aryl(trialkoxy)silanes in good yields.

TABLE 3. Optimization of Reaction Conditions on Hiyama Reaction[a]



4a

entry	ligand	time (h)	solvent	Pd source	yield (%)[b]
1	 **1a**	20	Dioxane	$Pd(OAc)_2$	55
2	 **1b**	20	Dioxane	$Pd(OAc)_2$	49
3	 **1d**	20	Dioxane	$Pd(OAc)_2$	57
4	 **2a**	20	Dioxane	$Pd(OAc)_2$	23
5	 **2b**	20	Dioxane	$Pd(OAc)_2$	45
6	**1d**	20	^{t}BuOH	$Pd(OAc)_2$	0
7	**1d**	20	DMF	$Pd(OAc)_2$	38
8	**1d**	20	DMSO	$Pd(OAc)_2$	40
9	**1d**	5	*m*-Xylene	$Pd(OAc)_2$	54
10	**1d**	5	PhMe	$Pd(OAc)_2$	68
11	–	5	PhMe	$Pd(OAc)_2$	58
12	**1d**	5	PhMe	$Pd(dba)_2$	82
13	**1d**	5	PhMe	$PdCl_2(MeCN)_2$	79
14	**1d**	**5**	**PhMe**	**$PdCl_2$**	**83(76)**[c]

[a] Reaction conditions: p-bromoacetophenone (0.5 mmol), phenyl(triethoxy)silane (1.0 mmol), TBAF (1.0 mmol) in THF (1 M, 1 mL), solvent (1.5 mL), palladium source (0.02 mmol), ligand (0.03 mmol). [b] GC yields. [c] Isolated yields.

Experimental Section

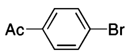
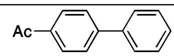
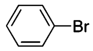
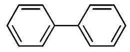
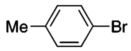
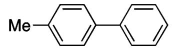
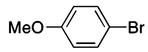
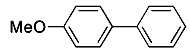
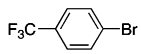
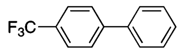
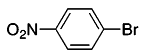
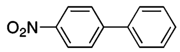
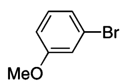
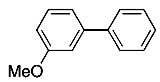
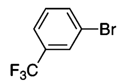
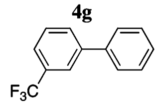
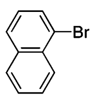
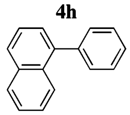
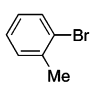
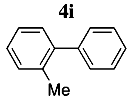
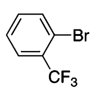
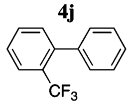
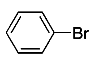
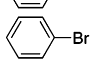
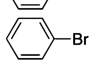
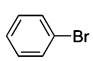
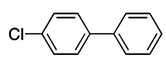
Preparation of Glyoxal Bis(*N*-methyl-*N*-3-tolylhydrazone) (1c). A solution of *N*-methyl-*N*-3-tolylhydrazine (0.163 g, 1.2 mmol) in MeOH (2 mL) was added to 40 wt % of glyoxal in water (0.073 g, 0.5 mmol) at 0 °C. The mixture was stirred for 5.5 h at room temperature. The yellow solid precipitated and was collected by filtration, washed with hexane, and dried under reduced pressure: 0.140 g, 0.48 mmol, 95% as a yellow solid; mp 157–159 °C; IR-(KBr) 1542 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 6H), 3.37 (s, 6H), 6.71–6.81 (m, 2H), 7.03–7.11 (m, 2H), 7.14–7.23 (m, 4H), 7.51 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 21.8, 33.5, 112.4, 116.1, 121.7, 128.9, 133.7, 138.9, 147.6; FAB-MS *m/z* (rel. intens.) 294 (M^+, 80); HRMS (FAB-MS) *m/z* calcd for $C_{18}H_{22}N_4$ 294.1844, found 294.1818.

Preparation of *N*,*N*-Bis(indolin-1-yl)ethane-1,2-diimine (1d). A solution of *N*-aminoindoline (1.47 g, 11 mmol) in MeOH (5 mL) was added to 40 wt % of glyoxal in water (0.725 g, 5 mmol) at 0 °C. The mixture was stirred for 3 h at room temperature. The yellow solid precipitated and was collected by filtration, washed with hexane, and dried under reduced pressure: 1.349 g, 4.65 mmol, 93% as a yellow solid; mp 251–253 °C; IR(KBr) 1532 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.81 (t, J = 7.3 Hz 2H), 3.19–3.25 (m, 4H), 3.80–3.86 (m, 4H), 7.07–7.19 (m, 6H), 7.34(s, 2H); ^{13}C NMR ($CDCl_3$) δ 27.0, 48.2, 108.6, 120.3, 124.8, 127.5, 127.8, 134.4, 147.5; EI-

(11) For reviews, see: (a) Hiyama, T. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Weinheim, Germany, 1998. (b) Hiyama, T. *J. Organomet. Chem.* **2002**, *653*, 58. (c) Denmark, S. E.; Sweiss, R. F. *Acc. Chem. Res.*, **2002**, *35*, 835. (d) Spivey, A. C.; Gripton, C. J. G.; Hannah, J. P. *Curr. Org. Synth.* **2004**, *1*, 211.

(12) (a) Gouda, K.; Hagiwara, E.; Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1996**, *61*, 7232. (b) Pilcher, A. S.; DeShong, P. *J. Org. Chem.* **1996**, *61*, 6901. (c) Hagiwara, E.; Gouda, K.; Hatanaka, Y.; Hiyama, T. *Tetrahedron Lett.* **1997**, *38*, 439. (d) Brescia, M.-R.; DeShong, P. *J. Org. Chem.* **1998**, *63*, 3156. (e) Mowery, M. E.; DeShong, P. *J. Org. Chem.* **1999**, *64*, 3266. (f) Mowery, M. E.; DeShong, P. *Org. Lett.* **1999**, *1*, 2137. (g) Mowery, M. E.; DeShong, P. *J. Org. Chem.* **1999**, *64*, 1684. (h) Denmark, S. E.; Wu, Z. *Org. Lett.* **1999**, *1*, 1495. (i) Denmark, S. E.; Choi, J. Y. *J. Am. Chem. Soc.* **1999**, *121*, 5821. (j) Li, J.-H.; Deng, C.-L.; Liu, W.-J. Xie, Y.-X. *Synthesis* **2005**, 3039. (k) Donmin, D.; Benito-Garagorri, D.; Mereiter, K.; Fröhlich, J.; Kirchner, K. *Organometallics* **2005**, *24*, 3957. (l) Li, J.-H.; Deng, C.-L.; Xie, Y.-X. *Synthesis* **2006**, 969.

TABLE 4. Hiyama Reaction of Aryl Bromides with Siloxanes[a]

entry	aryl bromide	siloxane	time (h)	product	yield (%)[b]
1		$PhSi(OEt)_3$	5		76
2		$PhSi(OEt)_3$	3		73
3		$PhSi(OMe)_3$	3	**4a**	69
4		$PhSi(OEt)_3$	3	 **4b**	80
5		$PhSi(OEt)_3$	3	 **4c**	64
6		$PhSi(OEt)_3$	3	 **4d**	63
7		$PhSi(OEt)_3$	3	 **4e**	87
8		$PhSi(OEt)_3$	3	 **4f**	70
9		$PhSi(OEt)_3$	3	 **4g**	74
10		$PhSi(OEt)_3$	3	 **4h**	74
11		$PhSi(OEt)_3$	3	 **4i**	72
12[c]		$PhSi(OEt)_3$	3	 **4j**	60
13[c]		$PhSi(OEt)_3$	3	 **4k**	50
14		*p*-$MePhSi(OEt)_3$	3	**4c**	71
15		*p*-$MeOPhSi(OEt)_3$	3	**4d**	58
16		*p*-$CF_3PhSi(OEt)_3$	3	**4e**	90
17		*p*-$ClPhSi(OEt)_3$	3	 **4l**	79

[a] Reaction conditions: aryl bromide (0.5 mmol), siloxane (1.0 mmol), TBAF (1.0 mmol) in THF (1 M, 1 mL), PhMe (1.5 mL), $PdCl_2$ (0.02 mmol), ligand **1d** (0.03 mmol). [b] Isolated yields. [c] This reaction used 3 equiv of phenyl(triethoxy)silane.

MS *m*/*z* (rel. intens.): 290 (M^+, 24); HRMS (FAB-MS) *m*/*z* calcd for $C_{18}H_{18}N_4$ 290.1531, found 290.1531; X-ray diffraction analysis data of **1d** (Figure S1 of the Supporting Information). Yellow cubic crystals from hexane−chloroform, monoclinic space group $P2_1/c$, $a = 12.9030(4)$ Å, $b = 10.4680(3)$ Å, $c = 11.7384(4)$ Å, $\alpha = 90°$, $\beta = 112.6840(10)°$, $\gamma = 90°$, $V = 1462.84(8)$ Å^3, $Z = 4$, $\rho = 1.318$ g/cm^3, μ (Mo Kα) = 0.81 cm^{-1}. The structure was solved by the direct method of full matrix least-squares, where the final R and R_w were 0.051 and 0.168 for 5462 reflections, respectively.

Preparation of *N*-(Indolin-1-yl)(pyridin-2-yl)methanimine (2b). Under an atmosphere of argon, a solution of *N*-aminoindoline (0.067 g, 0.5 mmol) in MeOH (1.5 mL) was added to 2-pyridinecarboxaldehyde (0.032 g, 0.3 mmol) at room temperature. The mixture was stirred for 24 h at 50 °C. The mixture was directly concentrated under reduced pressure. The residue was purified by silica gel chromatography (hexane/EtOAc = 1/1): 0.022 g, 0.10 mmol, 33% as a yellow solid; mp 111−112 °C; IR(KBr) 1557 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.27 (t, J = 8.3 Hz, 2H), 3.92 (t, J = 8.2 Hz, 2H), 6.86 (dt, J = 1.4 and 7.2 Hz, 1H), 7.11−7.26 (m, 5H), 7.46 (s, 1H), 7.66 (dt, J = 1.7 and 7.7 Hz, 1H), 8.01 (d, J = 8.1 Hz, 1H), 8.52 (d, J = 4.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 27.1, 48.0, 109.1, 118.9, 120.9, 121.9, 125.0, 127.8, 127.9, 133.3, 136.1, 147.3, 149.1, 155.6; EI-MS *m*/*z* (rel. intens.): 223 (M^+, 18); HRMS (FAB-MS) *m*/*z* calcd for $C_{14}H_{13}N_3$ + H 224.1188, found 224.1182.

Sonogashira Cross-Coupling Reaction of Aryl Halides with Alkynes (Table 2). Under an atmosphere of argon, alkyne (1.2 mmol) was added to the mixture of aryl halide (1 mmol), K_3PO_4 (1.4 mmol), $PdCl_2(MeCN)_2$ (0.02 mmol), ligand (0.02 mmol), and CuI (0.05 mmol) in DMF (2 mL) at room temperature. The mixture was stirred at 80 °C. After 5 h, the mixture was diluted with ethyl acetate and water. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography.

(4-Fluorophenyl)-4-tolylacetylene (3j). 70% as a white solid; mp 91−92 °C; IR (KBr) 2216 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 2.36 (s, 3H), 6.96−7.08 (m, 2H), 7.15 (d, J = 7.84 Hz, 2H), 7.41 (d, J = 7.65 Hz, 2H), 7.42−7.52 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.5, 87.6, 89.2 (d, J = 1.1 Hz), 115.6 (d, J = 22.1 Hz), 119.6 (d, J = 3.5 Hz), 120.0, 129.1, 131.4, 133.4 (d, J = 8.3 Hz), 138.5, 162.4 (d, J = 249.2 Hz); EI-MS *m*/ *z* (rel. intens.): 210 (M^+, 100); HRMS (FAB-MS) *m*/*z* calcd for $C_{15}H_{11}F$ 210.0845, found 210.0840.

(2-Fluorophenyl)-4-tolylacetylene (3l). 95% as a white solid; mp 55−56 °C; IR (KBr) 2219 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 3H), 7.05−7.19 (m, 4H), 7.22−7.35 (m, 1H), 7.41−7.56 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 21.5, 82.0, 94.6 (d, J = 3.2 Hz), 112.1 (d, J = 15.6 Hz), 115.5 (d, J = 21.0 Hz), 119.8, 123.9 (d, J = 3.7 Hz), 129.1, 129.7 (d, J = 8.0 Hz), 131.6, 133.4 (d, J = 0.9 Hz), 138.8, 162.6 (d, J = 251.3 Hz); EI-MS *m*/*z* (rel. intens.): 210 (M^+, 100); HRMS (FAB-MS) *m*/*z* calcd for $C_{15}H_{11}F$ 210.0845, found 210.0833.

6-*p*-Tolylhex-5-yl-1-ol (3m). 73% as a colorless liquid; IR (KBr) 2231 and 3357 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.46 (s, 1H), 1.58−1.82 (m, 4H), 2.33 (s, 3H), 2.45 (t, J = 6.6 Hz, 2H), 3.71 (t, J = 6.1 Hz, 2H), 7.08 (d, J = 7.9 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 19.2, 21.4, 25.0, 31.9, 62.5, 80.9, 89.0, 120.7, 128.9, 131.4, 137.5; EI-MS *m*/*z* (rel. intens.): 188 (M^+, 15); HRMS (FAB-MS) *m*/*z* calcd for $C_{13}H_{16}O$ 188.1201, found 188.1205.

Hiyama Cross-Coupling Reaction of Aryl Bromides with Siloxanes (Table 4). Under an atmosphere of argon, siloxane (1.0 mmol) and TBAF (1.0 mmol) in THF (1 M, 1 mL) were added to the mixture of aryl bromide (0.5 mmol), $PdCl_2$ (0.02 mmol), and ligand (0.03 mmol) in PhMe (1.5 mL) at room temperature. The mixture was stirred at 80 °C. After 3 h, the mixture was diluted with ethyl acetate and water. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography.

Acknowledgment. This work was supported in part by a Grant-in-Aid for Scientific Research (No. 16750070) from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Supporting Information Available: ORTEP drawing **1d** (Figure S1), ^{1}H and ^{13}C NMR spectra of all compounds, and X-ray crystallographic file (CIF) for **1d**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO061734I