

# Palladium-Catalyzed Coupling Reaction of Terminal Alkynes with Aryl Iodides in the Presence of Indium Tribromide and Its Application to a One-Pot Synthesis of 2-Phenylindole

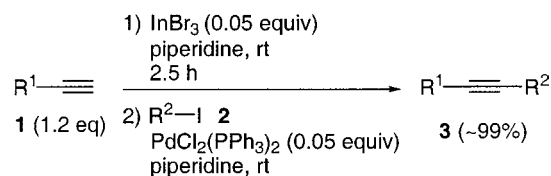
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Received December 24, 2003

## ABSTRACT



The use of a novel  $\text{PdCl}_2(\text{PPh}_3)_2\text{—InBr}_3$  reagent system to catalyze cross-coupling reactions of a variety of aryl iodides with several terminal alkynes is described. The corresponding functional alkyne derivatives were produced in good to excellent yields. Moreover, a catalytic amount of  $\text{InBr}_3$  effectively catalyzes the intramolecular cycloaddition of 2-phenylethynylaniline to form an indole skeleton in high yield.

The transition metal-catalyzed cross-coupling reaction of metal acetylides with vinyl/aryl halides is one of the most important reactions in organic synthesis, since it provides a useful method for direct  $\text{sp}^2\text{—sp}^2$  carbon—carbon bond formation.<sup>1</sup> Palladium-catalyzed cross-coupling reactions of terminal alkynes with vinyl/aryl halides in the presence of  $\text{CuI}$  (Sonogashira–Hagihara alkynylation)<sup>2a–e</sup> or in the absence of any cocatalyst (Heck alkynylation)<sup>2f,g</sup> are more useful

synthetically and have been widely used in the synthesis of a variety of polyfunctional alkynes. Since the initial report describing both reactions,<sup>2</sup> many chemists have reported the use of novel metal acetylides, which function as a synthetically more useful tool than copper acetylide,<sup>1c,3</sup> and the development of a more active palladium catalyst for cross-coupling with unactivated arenes such as aryl bromides and chlorides.<sup>4</sup> On the other hand, indium(III) halide has recently

(1) For selected reviews of metal-catalyzed coupling reactions, see: (a) Negishi, E. Xu, C. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Eds.; Wiley-Interscience: New York, 2002; p 531. (b) Sonogashira, K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol 3, p 521. (c) Negishi, E.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979 and refs cited therein.

(2) For selected reviews and papers on the Sonogashira alkynylation and the Heck alkynylation, see: (a) Sonogashira, K. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Eds.; Wiley-Interscience: New York, 2002; p 493. (b) Tykwinski, R. R. *Angew. Chem., Int. Ed.* **2003**, *42*, 1566 and refs cited therein. (c) Sonogashira, K. *J. Organomet. Chem.* **2002**, *653*, 46. (d) Takahashi, S.; Kuroyama, K.; Sonogashira, K. Hagihara, N. *Synthesis* **1980**, 627. (e) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467. (f) Dieck, H. A.; Heck, F. R. *J. Organomet. Chem.* **1975**, *93*, 259. (g) Cassar, L. J. *Organomet. Chem.* **1975**, *93*, 253.

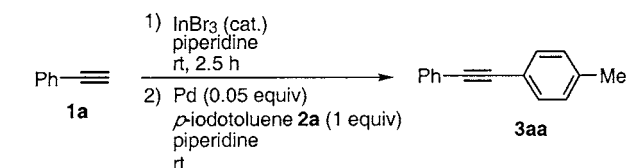
(3) For selected papers and reviews of the Pd-catalyzed coupling reaction of alkynylmetal compounds with aryl halides, see the following. For Zn: (a) Negishi, E.; Qian, M.; Zeng, F.; Anastasia, L.; Babinski, D. *Org. Lett.* **2003**, *5*, 1597. (b) Crisp, G. T.; Turner, P. D.; Stephens, K. A. *J. Organomet. Chem.* **1998**, *570*, 219. (c) Negishi, E.; Kotori, M.; Xu, C. *J. Org. Chem.* **1997**, *62*, 8957. (d) Yoneda, N.; Matsuoka, S.; Miyaura, N.; Fukuhara, T.; Suzuki, A.; *Bull. Chem. Soc. Jpn.* **1990**, *63*, 2124. For Sn: (e) Hatanaka, Y.; Matsui, K.; Hiyama, T. *Tetrahedron Lett.* **1989**, *30*, 2403. (f) Kosugi, M.; Tamura, H.; Sano, H.; Migita, T. *Chem. Lett.* **1987**, 193. (g) Stille, J. K.; Simpson, J. H. *J. Am. Chem. Soc.* **1987**, *109*, 2138. For B: (h) Oh, C. H.; Jung, S. H.; *Tetrahedron Lett.* **2000**, *41*, 8513. (i) Fürstner, A.; Seidel, G. *Tetrahedron* **1995**, *51*, 11165. For Al: (j) Gelman, D.; Tsvetikhovskiy, D.; Molander, G. A.; Blum, J. *J. Org. Chem.* **2002**, *67*, 6287. (k) Negishi, E. *Acc. Chem. Res.* **1982**, *15*, 340. For Si: (l) Nishihara, Y.; Ikegashira, K.; Hirabayashi, K.; Ando, J.-I.; Morio, A.; Hiyama, T. *J. Org. Chem.* **2000**, *65*, 1780.

attracted considerable attention in synthetic organic chemistry due to the fact that it has a lower toxicity than organic tin compounds, a high stability under aqueous conditions, and a strong tolerance to oxygen- and nitrogen-containing reaction substrates and functional groups.<sup>5</sup> Although a number of synthetic applications using indium halide have been reported,<sup>6</sup> the transition metal-catalyzed cross-coupling reaction of terminal alkynes with organic halides in the presence of a catalytic amount of an indium halide as a typical Sonogashira reaction has not been extensively studied.<sup>7</sup> In this regard, Alami and Linstrumelle et al. reported the simple and efficient coupling of terminal alkynes with aryl halides using Pd(PPh<sub>3</sub>)<sub>4</sub> in a cyclic secondary amine,<sup>8</sup> and we have also reported that indium tribromide readily promotes the alkylation of a variety of aldehydes with several terminal alkynes in the presence of triethylamine to give the corresponding propargylic alcohols.<sup>9</sup> To expand on this approach further, we attempted to apply the method to the novel transition metal-catalyzed cross-coupling of 1-alkynes with aryl halides in the presence of an indium catalyst. In this communication, we describe some preliminary results, in which a novel PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>–InBr<sub>3</sub> reagent system effectively catalyzes the cross-coupling of terminal alkynes with aryl iodides leading to the corresponding functional alkyne derivatives in excellent yields. We also disclose herein that indium(III) bromide catalyzes the smooth intramolecular

cyclization of 2-phenylethynylaniline, directly producing 2-phenylindole in good yield.

We initially examined the Pd-catalyzed cross-coupling reaction of phenylacetylene (**1a**) with *p*-iodotoluene (**2a**) in the presence of a catalytic amount of indium tribromide. When the terminal alkyne **1a** was treated with InBr<sub>3</sub> (20 mol %) in piperidine at room temperature for 2.5 h, followed by the addition of a piperidine solution of Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol %) and *p*-iodotoluene, the expected coupling adduct **3aa** was produced in 94% yield within 1 h (run 1 in Table 1).<sup>10</sup> A

**Table 1.** Examination of Indium Bromide and Reaction Conditions<sup>a</sup>



run	<b>1a</b> (equiv)	InBr <sub>3</sub> (equiv)	Pd	time (h)	yield (%) <sup>b</sup>
1	1	0.2	Pd(PPh <sub>3</sub> ) <sub>4</sub>	1	94
2	1	0.05	Pd(PPh <sub>3</sub> ) <sub>4</sub>	2	72
3	1	0.2	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	2	87
4	1.2	0.2	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	<0.2	99
5	<b>1.2</b>	<b>0.05</b>	<b>PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub></b>	<b>&lt;0.2</b>	<b>95</b>
6	1	none	Pd(PPh <sub>3</sub> ) <sub>4</sub>	2	70
7	1.2	none	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	5	89

<sup>a</sup> Reaction was carried out using phenylacetylene (**1a**, 0.48 mmol), *p*-iodotoluene (**2a**, 0.4 mmol), Pd catalyst (0.02 mmol), InBr<sub>3</sub> (0–0.2 equiv per equiv of **2a**), and piperidine (2.5 mL). <sup>b</sup> NMR yields based on *p*-iodotoluene.

catalytic amount of the indium catalyst (5 mol %) permitted the desired coupling reaction to proceed, but the product yield was decreased slightly (run 2). Similarly, when the coupling was carried out using PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> in place of Pd(PPh<sub>3</sub>)<sub>4</sub>, the corresponding alkyne was obtained in good yield (run 3).<sup>11</sup> By increasing the amount of alkyne **1a** used to 1.2 equiv per equivalent of the halide, the yield of bisarylalkyne **3aa** was increased to near quantitative. Moreover, in the case of PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, the presence of only 5 mol % indium bromide led to a smooth reaction that was complete within 15 min, to afford the expected product in excellent yield (run 5).<sup>12</sup> On the other hand, when Pd-catalyzed cross-coupling reactions were conducted without the indium catalyst under the above conditions, the reaction time needed to be extended, and the product yield was clearly reduced (runs 6 and 7).<sup>8b</sup> This result clearly shows that indium bromide functions as an effective cocatalyst in promoting this coupling reaction.<sup>13</sup>

(10) With amines as the solvent, a reaction using pyrrolidine gave a similar result (72% under the same conditions in run 1, Table 1), although coupling reactions using other amines such as triethylamine and diethylamine did not proceed and the starting materials were recovered.

(11) Other catalysts such as Pd(OAc)<sub>2</sub> and NiCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> were not effective for this reaction.

(12) Coupling reaction using CuI instead of InBr<sub>3</sub> showed a similar result. For example, the reaction using **2a** was complete within 15 min and the yield of product **3aa** was 98%.

(4) For selected recent advantages of the Sonogashira-type reaction, (a) see ref 2b. (b) Soheili, A.; Albaneze-Walker, J.; Murry, J. A.; Dormer, P. G.; Hughes, D. L. *Org. Lett.* **2003**, 5, 4191. (c) Méry, D.; Heuzé, K.; Astruc, S. *Chem. Commun.* **2003**, 1934. (d) Köllhofer, A.; Pullmann, T.; Plenio, H. *Angew. Chem., Int. Ed.* **2003**, 42, 1056. (e) Eckhardt, M.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, 125, 13642. (f) Remmele, H.; Köllhofer, A.; Plenio, H. *Organometallics* **2003**, 22, 4098. (g) Yang, C.; Nolan, S. P. *Organometallics* **2002**, 21, 1020. (h) Batey, R. A.; Shen, M.; Lough, A. *Org. Lett.* **2002**, 4, 1411. (i) Eberhard, M. R.; Wang, Z.; Jensen, C. M. *Chem. Commun.* **2002**, 818. (j) Alami, M.; Crousse, B.; Ferri, F. *J. Organomet. Chem.* **2001**, 624, 114. (k) Hundertmark, T.; Littke, A. F.; Buchwald, S. L.; Fu, G. C. *Org. Lett.* **2000**, 2, 1729. (l) Thorand, S.; Krause, N. *J. Org. Chem.* **1998**, 63, 8551.

(5) (a) Bandini, M.; Melchiorre, P.; Melloni, A.; Umani-Ronchi, A. *Synlett* **2002**, 1110. (b) Onishi, Y.; Ito, T.; Yasuda, M.; Baba, A. *Eur. J. Org. Chem.* **2002**, 1578. (c) Nagarajan, R.; Perumal, P. T. *Tetrahedron* **2002**, 58, 1229. (d) Yadav, J. S.; Abraham, S.; Reddy, B. V. S.; Sabitha, R. G. *Synthesis* **2001**, 2165. (e) Takami, K.; Yorimitsu, H.; Shinokubo, H.; Matsubara, S.; Oshima, K. *Org. Lett.* **2001**, 3, 1997. (f) Chauhan, K. K.; Frost, C. G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3015. (g) Tsuchimoto, T.; Maeda, T.; Shirakawa, E.; Kawakami, Y. *Chem. Commun.* **2000**, 1573. (h) Ranu, B. C. *Eur. J. Org. Chem.* **2000**, 2347. (i) Araki, S.; Kamei, T.; Hirashita, T.; Yamamura, H.; Kawai, M. *Org. Lett.* **2000**, 2, 847. (j) Yasuda, M.; Miyai, T.; Shibata, I.; Baba, A.; Nomura, R.; Matsuda, H. *Tetrahedron Lett.* **1995**, 36, 9497. (k) Marshall, J. A.; Hinkle, K. W. *J. Org. Chem.* **1995**, 60, 1920.

(6) (a) Lee, P. H.; Lee, S. W.; Seomoon, D. *Org. Lett.* **2003**, 5, 4963. (b) Lehman, U.; Awasthi, S.; Minehan, T. *Org. Lett.* **2003**, 5, 2405. (c) Takami, K.; Mikami, S.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *J. Org. Chem.* **2003**, 68, 6627. (d) Rodríguez, D.; Sestelo, J. P.; Sarandeses, L. A. *J. Org. Chem.* **2003**, 68, 2518. (e) Lee, K.; Lee, J.; Lee, P. H. *J. Org. Chem.* **2002**, 67, 8265. (f) Pena, M. A.; Pérez, I.; Pérez Sestelo, J.; Sarandeses, L. A. *Chem. Commun.* **2002**, 2246. (g) Pérez, I.; Pérez Sestelo, J.; Sarandeses, L. A. *J. Am. Chem. Soc.* **2001**, 123, 4155. (h) Pérez, I.; Pérez Sestelo, J.; Sarandeses, L. A. *Org. Lett.* **1999**, 1, 1267.

(7) During our submission, Negishi et al. also reported a similar effect of InCl<sub>3</sub> as a cocatalyst in Pd-catalyzed cross-coupling reaction; see: Qian, M.; Huang, Z.; Negishi, E. *Org. Lett.* **2004**, 6, 1531.

(8) (a) Alami, M.; Ferri, F.; Linstrumelle, G. *Tetrahedron Lett.* **1993**, 34, 6403. (b) Leadbeater and Tominack recently reported on the PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> catalyzed-coupling reaction of terminal alkynes with aryl halides/triflates without CuI in a cyclic amine; see: Leadbeater, N. E.; Tominack, B. J. *Tetrahedron Lett.* **2003**, 44, 4233.

(9) Sakai, N.; Hirasawa, M.; Konakahara, T. *Tetrahedron Lett.* **2003**, 44, 4171.

To extend the general applicability of this coupling reaction, the reaction of several 1-alkynes with various aryl iodides was carried out under the above-optimized conditions, the results of which are summarized in Table 2. In most of

**Table 2.** Pd–In Catalyzed Cross-Coupling of Terminal Alkynes with Aryl Iodides

$\text{R}^1\text{—}\text{C}\equiv\text{C—H} \xrightarrow[\text{2) R}^2\text{—I, 2) PdCl}_2(\text{PPh}_3)_2 \text{ (0.05 equiv), piperidine, rt}]{\text{1) InBr}_3 \text{ (0.05 equiv), piperidine, rt, 2.5 h}} \text{R}^1\text{—}\text{C}\equiv\text{C—R}^2$				
run	R <sup>1</sup>	R <sup>2</sup>	time (h)	product, yield (%) <sup>a</sup>
1	Ph <b>1a</b>	<i>p</i> -Me-C <sub>6</sub> H <sub>4</sub> <b>2a</b>	<0.2	<b>3aa</b> , 95 <sup>b</sup>
2	Ph	<i>o</i> -Me-C <sub>6</sub> H <sub>4</sub> <b>2b</b>	8	<b>3ab</b> , 55 <sup>b,d</sup>
3	Ph	<i>p</i> -NH <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> <b>2c</b>	1.5	<b>3ac</b> , 96
4	Ph	<i>o</i> -NH <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> <b>2d</b>	1	<b>3ad</b> , 99 <sup>b</sup>
5	Ph	<i>p</i> -MeO-C <sub>6</sub> H <sub>4</sub> <b>2e</b>	<0.5	<b>3ae</b> , 99 <sup>b</sup>
6	Ph	<i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> <b>2f</b>	<0.5	<b>3af</b> , 99
7	Ph	<i>p</i> -F-C <sub>6</sub> H <sub>4</sub> <b>2g</b>	<0.2	<b>3ag</b> , 93
8	C <sub>6</sub> H <sub>13</sub> <b>1b</b>	<i>p</i> -Me-C <sub>6</sub> H <sub>4</sub> <b>2a</b>	6 <sup>c</sup>	<b>3ba</b> , 93 <sup>b</sup>
9	C <sub>6</sub> H <sub>13</sub>	<i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> <b>2f</b>	4	<b>3bf</b> , 88
10	Me <sub>3</sub> Si <b>1c</b>	<i>p</i> -MeO-C <sub>6</sub> H <sub>4</sub> <b>2e</b>	6	<b>3ce</b> , 79 <sup>e</sup>
11	Me <sub>3</sub> Si	<i>o</i> -NH <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> <b>2d</b>	3	<b>3cd</b> , 74
12	Me <sub>3</sub> Si	<i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> <b>2f</b>	1	<b>3cf</b> , 99
13	<i>t</i> -Bu <b>1d</b>	<i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> <b>2f</b>	3	<b>3df</b> , 95
14	Ph <b>1a</b>	2-thienyl <b>2h</b>	9	<b>3ah</b> , 85

<sup>a</sup> Isolated yields based on aryl halide. <sup>b</sup> NMR yields based on the aryl halide. <sup>c</sup> Reaction temperature = 60 °C. <sup>d</sup> Pd-catalyzed coupling reaction without a cocatalyst, as CuI gave no product; see ref 7b. <sup>e</sup> Pd-catalyzed coupling reaction without a cocatalyst, as CuI gave the product in 28% yield; see ref 8b.

the cases where phenylacetylene (**1a**) was used, the Pd-coupling reactions were complete in a short time (<1.5 h), and the corresponding alkynes **3** were produced in high yields (runs 1, 3–7, and 14), except for the reaction in which *o*-iodotoluene was used (**2b**) (run 2). In addition, the catalytic system described here could be adapted to reactions employing other alkynes such as 1-octyne (**1b**), trimethylsilylacetylene (**1c**), and *tert*-butylacetylene (**1d**) (runs 8–13). It is noteworthy that utilizing this improved procedure dramatically improved the yields of the coupling adducts **3ab** and **3ce** in comparison to those reported in the recent literature (**3ab**, 0%; **3ce**, 28%) (runs 2 and 10).<sup>8b</sup>

The intramolecular cyclization of 2-phenylethynylaniline (**3ad**) in the presence of indium bromide or other catalysts was next examined, and the results are listed in Table 3. As a result of these experiments, we found that when 1 equiv of indium bromide per equiv of **3ad** is used in toluene, the intramolecular cyclization of **3ad** is essentially complete within 10 min, producing a nearly quantitative yield of 2-phenylindole (**4**) (run 1).<sup>14</sup> Moreover, decreasing the

(13) When the reaction using InCl<sub>3</sub> instead of InBr<sub>3</sub> was carried out, the reaction time was prolonged (5 h) and the product yield of **3aa** was decreased to 68%.

**Table 3.** Examination of the Intramolecular Cyclization of 2-Phenylethynylaniline

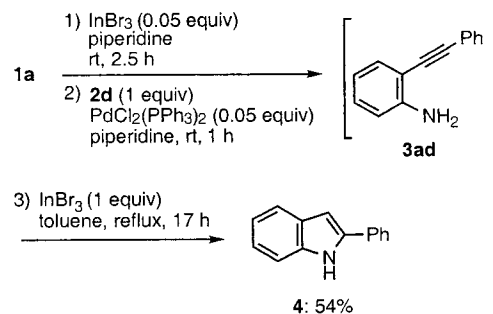
$\text{3ad} \xrightarrow[\text{solvent, temp}]{\text{catalyst}} \text{4}$					
run	catalyst (equiv)	solvent	temp (°C)	time (h)	yield (%) <sup>a</sup>
1	InBr <sub>3</sub> ( <b>1</b> )	toluene	reflux	<0.2	<b>99</b>
2	InBr <sub>3</sub> (0.05)	toluene	reflux	1	95
3		toluene	reflux	24	18
4	InBr <sub>3</sub> (0.05)	toluene	rt	24	15
5	InBr <sub>3</sub> (0.05)	piperidine	reflux	24	9
6		piperidine	reflux	24	10
7	Cu(OTf) (1)	toluene	reflux	10	nd <sup>b</sup>
8	Pd(II) (0.05) <sup>c</sup>	toluene	reflux	12	75

<sup>a</sup> NMR yield based on **3ad**. <sup>b</sup> nd = not detected. <sup>c</sup> Pd(II) = PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>.

amount of the indium catalyst to less than 0.05 equiv per equiv of **3ad** also gave a similar result (run 2). A Pd(II) catalyst also catalyzed the cyclization in mild yield (run 7).<sup>15</sup> In contrast, in the case of Cu(OTf)<sub>2</sub>,<sup>16</sup> the formation of cycloadduct **4** could not be confirmed because of product decomposition under the reflux conditions employed. These results imply that an initial coordination of an alkyne  $\pi$ -bond with InBr<sub>3</sub> increases the electrophilicity of the alkyne unit, facilitating subsequent intramolecular nucleophilic attack onto the alkyne carbon by the ortho amine group.<sup>17</sup>

Finally, we applied the present method to a one-pot synthesis of 2-phenylindole (**4**). As shown in Scheme 1, the

**Scheme 1.** One-Pot Synthesis of 2-Phenylindole



Pd-catalyzed reaction of phenylacetylene (**1a**) with *o*-iodoaniline (**2d**) in the presence of InBr<sub>3</sub> (5 mol %) was initially carried out under the optimized conditions. The bisarylalkyne **3ad** formed was not isolated, and the solvent

(14) Intramolecular cycloaddition of **3cd** did not proceed at all.

(15) (a) Cacchi, S.; Fabrizi, G.; Parisi, L. M. *Org. Lett.* **2003**, *5*, 3843. (b) Hiroya, K.; Itoh, S.; Ozawa, M.; Kanamori, Y.; Sakamoto, T. *Tetrahedron Lett.* **2002**, *43*, 1277. (c) Ezquerro, J.; Pedregal, C.; Lamas, C.; Barluenga, J.; Pérez, M.; García-Martín, M. A.; González, J. M. J. *Org. Chem.* **1996**, *61*, 5804. (d) Villemain, D.; Goussu, D. *Heterocycles* **1989**, *29*, 1255.

was replaced with toluene. To this solution was added 1 equiv of indium bromide, and the toluene solution was refluxed for 17 h, giving the expected indole derivative **4** in 54% yield.

Although there is no clear explanation for the actual role of indium bromide at present, we assume that  $\text{InBr}_3$  initially coordinates to the alkyne  $\pi$  bond to increase the acidity of the terminal hydrogen, followed by abstraction of the proton by a mild base such as piperidine to facilitate formation of alkynylindium species.<sup>17</sup> The evidence for the initial complexation/coordination process of Lewis acidic  $\text{InBr}_3$  to the alkyne  $\pi$  bond is supported by the fact that the smooth  $\text{InBr}_3$ -catalyzed intramolecular cyclization of coupled product **3ad** led to indole **4**.

In summary, we demonstrate herein that a novel  $\text{PdCl}_2\text{-(PPh}_3)_2\text{-InBr}_3$  reagent system effectively catalyzes the cross-

coupling reaction of terminal alkynes with aryl iodides leading to the corresponding functionalized alkyne derivatives in excellent yields. Thus, the indium catalyst is a quite useful cocatalyst for promoting this type of coupling reaction. In addition, it was found that indium(III) bromide catalyzes the smooth intramolecular cyclization of ethynylaniline derivatives without the need for a protecting group on a nitrogen atom, directly producing an indole skeleton. Further investigation of the mechanism of this reaction is now in progress.

**Acknowledgment.** This work was partially supported by a grant from the Japan Private School Promotion Foundation and a grant for High Technology Research Centers of Private Universities.

**Supporting Information Available:** Experimental procedures and spectroscopic data of compounds **3** and **4**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(16) (a) Arcadi, A.; Cacchi, S.; Marinelli, F. *Tetrahedron Lett.* **1989**, 30, 2581. (b) Iritani, K.; Matsubara, S.; Utimoto, K. *Tetrahedron Lett.* **1988**, 29, 1799.

(17) Sirakawa et al. reported that  $\text{In(OTf)}_3$  coordinates onto alkyne  $\pi$ -electrons to activate subsequent nucleophilic reaction by aromatics; see: Tsuchimoto, T.; Maeda, T.; Sirakawa, E.; Kawakami, Y. *Chem. Commun.* **2000**, 1573.