

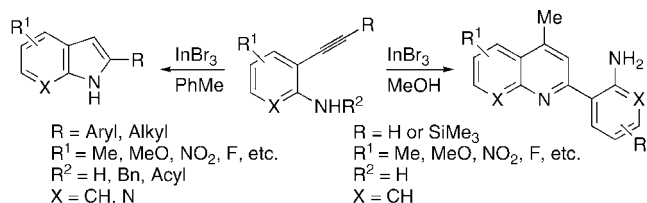
# InBr<sub>3</sub>-Promoted Divergent Approach to Polysubstituted Indoles and Quinolines from 2-Ethynylanilines: Switch from an Intramolecular Cyclization to an Intermolecular Dimerization by a Type of Terminal Substituent Group

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Use of a 2-ethynylaniline having an alkyl or aryl group on the terminal alkyne selectively produced a variety of polyfunctionalized indole derivatives in moderate to excellent yields via indium-catalyzed intramolecular cyclization of the corresponding alkynylaniline. In contrast, employment of a substrate with a trimethylsilyl group or with no substituent group on the terminal triple bond, exclusively afforded polysubstituted quinoline derivatives in good yields via indium-promoted intermolecular dimerization of the ethynylaniline. This indium catalytic system successfully accommodated the intramolecular cyclization of other arylalkyne skeletons involving a carboxylic acid and an amide group.

## Introduction

Polysubstituted indoles and quinolines have played an important and central role in biologically active substances and natural products.<sup>1</sup> Thus, development of facile and practical approaches to the synthesis of those skeletons has been investigated by a number of organic and pharmaceutical chemists.<sup>2</sup> Since development of the practical synthesis of indoles by Fischer et al., a number of the synthesis of indole derivatives has been widely investigated.<sup>2</sup> Particular attention has been paid to intramolecular cyclization of 2-alkynylanilines—one of the most convenient tools for preparation of polysubstituted indole derivatives.<sup>3</sup> For example, a combined method

consisting of a Pd/Cu-catalyzed Sonogashira reaction between an aryl halide and a terminal alkyne, and the subsequent intramolecular cyclization of the formed 2-ethynylaniline derivative with a palladium catalyst,<sup>4</sup> and the procedure using intramolecular cyclization of a 2-ethynylaniline derivative in the presence of various metal catalysts and metal complexes involving copper, gold, iridium, mercury, molybdenum, platinum, and rhodium also has been reported.<sup>5</sup> Moreover, an approach with bases, such as NaOEt,<sup>6</sup> *t*-BuOK,<sup>7</sup> KH,<sup>8</sup> and Et<sub>2</sub>Zn,<sup>9</sup> and Lewis acidic iodine complexes, such as I<sub>2</sub><sup>10</sup> and I(Py)<sub>2</sub>BF<sub>4</sub>,<sup>11</sup> via intramolecular cyclization also has been successful in the synthesis of an indole skeleton. On the other hand, facile and practical synthesis of the quinoline derivative, a basic

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framework widely found in naturally occurring products, biologically active substances, and clinical drugs, also has attracted considerable interest.<sup>12</sup> Therefore, a number of reactions involving the Conrad–Limpach–Knorr synthesis,<sup>13</sup> the Skraup synthesis,<sup>14</sup> and the Friedländer synthesis<sup>15</sup> have been developed for the preparation of this skeleton. Recently, the development of a modified Friedländer-type reaction using a Lewis acid has proven promising.<sup>16</sup> During the ongoing exploration of the novel synthetic process of nitrogen-containing heterocycles using an indium catalyst,<sup>17</sup> we also found that the structure of a terminal substituent on the triple bond bonded to an *o*-alkynylaniline directly has an effect on the selectivity of

### SCHEME 1. Representative Synthesis of the Substrates

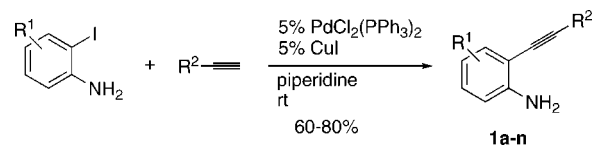
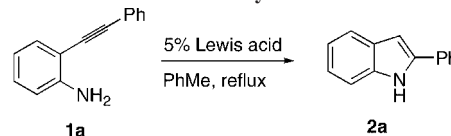


TABLE 1. Examination of a Catalyst



run	Lewis acid	time (h)	yield (%) <sup>a</sup>
1	BF <sub>3</sub> •OEt <sub>2</sub>	12	(22)
2	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub>	12	(29)
3	AlCl <sub>3</sub>	12	(31)
4	Cu(OTf) <sub>2</sub>	12	9
5	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	12	75
6	InBr <sub>3</sub>	1	(95)
7	InCl <sub>3</sub>	3	90
8	InI <sub>3</sub>	3	6
9	InBr <sub>3</sub> (1 equiv)	0.1	98
10	none	24	18

<sup>a</sup> NMR yield (isolated yield).

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the subsequent reaction path, resulting in the selective preparation of two quite different heterocycles.<sup>18</sup> Namely, a terminal group, such as an alkyl and an aryl group, predominately produces the corresponding indole derivatives via the indium-catalyzed *intramolecular cyclization* of the alkyne. In contrast, the reaction using the substrate with a trimethylsilyl group or with no substituent group on the terminal triple bond exclusively produced the multifunctionalized quinoline derivatives through indium-promoted *intermolecular dimerization* of the ethynylaniline derivative. Thus, the focus of our group's moved to the scope and limitations of both intramolecular cyclization and intermolecular dimerization from the original substrate. This paper details the results of a reinvestigation of indium-promoted reactions.

## Results and Discussion

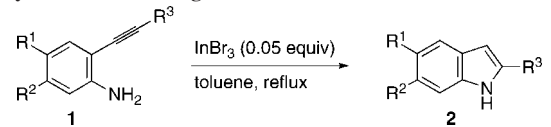
**In-Catalyzed Intramolecular Cyclization Leading to Indole Derivatives.** Initially, a series of 2-ethynylaniline derivatives **1a–n** as a reaction substrate were prepared via a Sonogashira-coupling reaction between 2-iodoaniline derivatives and several types of terminal alkynes (Scheme 1).<sup>19</sup>

To confirm the highly catalytic activity of an indium salt for the intramolecular cyclization of 2-phenylethynylaniline (**1a**), we then reinvestigated several types of Lewis acid for optimal conditions. For example, when the reaction using a catalytic amount of typical Lewis acids, such as BF<sub>3</sub>•OEt<sub>2</sub>, B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>, and AlCl<sub>3</sub>, was examined, the desired cyclization produced 2-phenylindole (**2a**), though the yield was rather low (Table 1, runs 1–3). Cu(OTf)<sub>2</sub>, which promoted a similar cyclization of an *N*-protected ethynylaniline,<sup>20</sup> did not show a catalytic effect to

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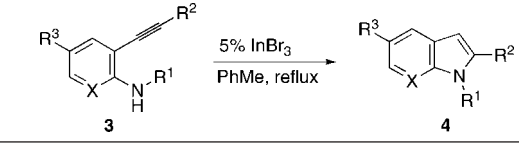
**TABLE 2.** In-Catalyzed Intramolecular Cyclization of Ethynylanilines **1** Leading to Indoles **3**


run	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>		time (h)	yield (%) <sup>a</sup>	
1	H	H	Ph	(1a)	0.5	95	(2a)
2	Me	H	Ph	(1b)	0.5	98	(2b)
3	Me	Me	Ph	(1c)	0.5	90	(2c)
4	NO <sub>2</sub>	H	Ph	(1d)	2	90	(2d)
5	F	H	Ph	(1e)	2	91	(2e)
6	CN	H	Ph	(1f)	2	98	(2f)
7	H	H	4-BuC <sub>6</sub> H <sub>4</sub>	(1g)	6	48	(2g)
8	Me	H	C <sub>6</sub> H <sub>13</sub>	(1h)	1	62	(2h)
9	Me	Me	C <sub>6</sub> H <sub>13</sub>	(1i)	1	52	(2i)
10	NO <sub>2</sub>	H	C <sub>6</sub> H <sub>13</sub>	(1j)	8	77	(2j)
11	F	H	C <sub>6</sub> H <sub>13</sub>	(1k)	8	86	(2k)
12	CN	H	C <sub>6</sub> H <sub>13</sub>	(1l)	7	89	(2l)
13	Me	H	<i>t</i> -Bu	(1m)	4	59	(2m)
14	H	H	<i>t</i> -Bu	(1n)	4	59	(2n)

<sup>a</sup> Isolated yield.

the cyclization at all (run 4). However, in the case of Pd(II) instead of Cu(II), the yield of indole **2a** increased to 75% (run 5). In contrast, when the reaction was conducted with InBr<sub>3</sub> under standard conditions, the desired cyclization was cleanly completed within an hour to produce indole **2a** in an excellent yield (run 6). InCl<sub>3</sub> also showed a similar catalytic effect for the reaction, though the reaction time was slightly prolonged (run 7). These results strongly indicate that indium bromide/chloride prefers coordinating on an alkyne  $\pi$ -bond to a basic primary amino group. On the other hand, employment of InI<sub>3</sub> remarkably reduced the chemical yield (run 8). The cyclization using a stoichiometric amount of indium bromide was quantitatively completed within 10 min (run 9). Without the indium catalyst, the reaction did not produce the desired product in a practical yield (run 10). Thus, we found that the indium salt highly and effectively promotes this type of intramolecular cyclization without the loss of the catalytic activity, and the toluene reflux conditions using 0.05 equiv of indium bromide shows the best result.

To extend the generality of this reaction, the cyclization of various *N*-unsubstituted ethynylaniline produced was carried out, and the results are summarized in Table 2. The cyclization of ethynylanilines having an electron-donating group, such as a methyl group, was completed in a very short time, producing the corresponding indole derivatives **2** in good to excellent yields (runs 1–3). When the substrates having an electron-withdrawing group, such as a nitro, a fluoro, and a cyano group on the benzene moiety, were employed, the reaction time was slightly prolonged due to a lowering of the nucleophilicity of the amino group, but the yields showed excellent results (runs 4–6). Thus, it was found that a sort of a substituted group on the benzene ring was ineffective for the yield of the intramolecular cyclization. On the other hand, a substrate having an aliphatic group on the terminal phenyl group reduced the yield to 48% (run 7). Although the reaction of substrates **1**, containing a hexyl group as a terminal substituent instead of the phenyl group, underwent cyclization to produce the desired polysubstituted indole derivatives in good yields (runs 8–12), the cyclization using a more bulky group, such as a *tert*-butyl group, produced the corre-

**TABLE 3.** Synthesis of a Variety of Indole Derivatives


run	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	X		time (h)	yield (%) <sup>a</sup>
1	PhCH <sub>2</sub>	Ph	H	CH	(3a)	1	78 (4a)
2	MeCO	Ph	H	CH	(3b)	2	71 (4b)
3	EtCO <sub>2</sub>	Ph	H	CH	(3c)	20	70 (4c)
4	H	(CH <sub>2</sub> ) <sub>4</sub> OH	H	CH	(3d)	8	70 (4d)
5	H	2-Py	H	CH	(3e)	72	23 (41) <sup>b</sup> (4e)
6	H	Ph	Me	N	(3f)	72	27 (46) <sup>b</sup> (4f)

<sup>a</sup> Isolated yield. <sup>b</sup> InBr<sub>3</sub> (0.2 equiv) was used.

sponding indoles in moderate yields, due to the steric effect between the bulky group and the amino group (runs 13 and 14).

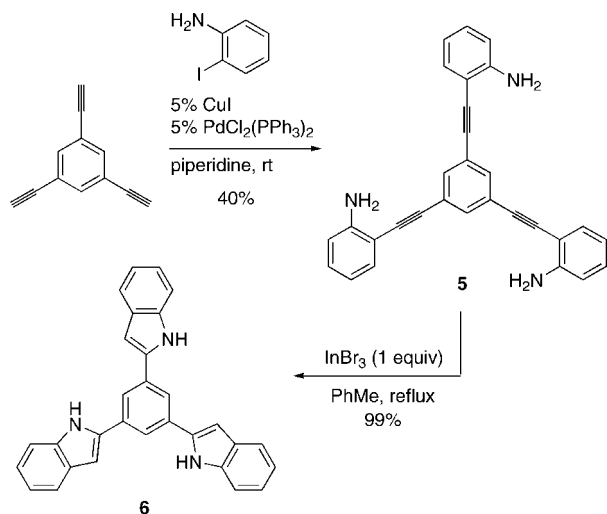
We then applied the present method to cyclize *N*-protected ethynylaniline that had a benzyl, an acetyl, and an ester group in the presence of the indium catalyst (Table 3). Initially, treatment of the reaction substrate having a benzyl group, with a 0.05 equivalent of InBr<sub>3</sub> produced the desired indole **4a** in a 78% yield (run 1). Similarly, when the reaction using the substrate with an acetyl group was also conducted, the cyclized product **4b** was obtained in a 71% yield within 2 h (run 2). Although cyclization with the ethynylaniline, which was substituted by a strong electron-withdrawing group, required a longer reaction time (>20 h) for the completion of the reaction, the reaction proceeded cleanly, producing the expected indole **4c** in a 70% yield (run 3). Interestingly, it was found that the introduction of a hydroxy group, which typically deactivates a common Lewis acid, on the terminal alkyne hardly affects the yield (run 4). Unfortunately, when the reaction was conducted with substrates **3e,f** having a pyridine ring, both cyclizations did not proceed smoothly, and the yields were extremely reduced to about 20% (runs 5 and 6). It seemed that InBr<sub>3</sub> prefers coordination on the more basic nitrogen atom in the pyridine ring to a softer base part, the C $\equiv$ C triple bond, resulting in the loss of its catalytic effect. Therefore, using a stoichiometric amount of InBr<sub>3</sub> unexpectedly resulted in the reaction leading to the formation of a complex mixture. Then, reducing the indium to a 0.2 equivalent in the intramolecular cyclization improved the yields to about 40%.<sup>21</sup>

Moreover, indium-promoted annulation of trialkynyltriamine was attempted (Scheme 2). Initially, *o*-iodoaniline was subjected to a Sonogashira-coupling reaction with trialkynylbenzene to produce the corresponding trialkynyltriamine **5** in a 40% yield. When the cyclization of **5** was then carried out using 1 equivalent of InBr<sub>3</sub> under the toluene reflux conditions, the expected triple-annulation proceeded simultaneously and cleanly to produce the desired 1,3,5-tris(2-indolyl)benzene **6** in a nearly quantitative yield.

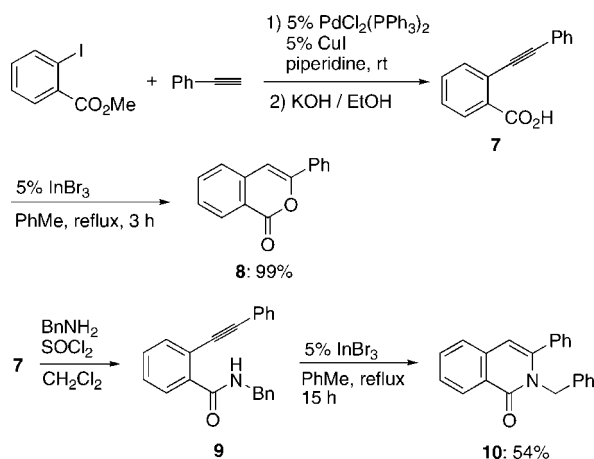
**In-Catalyzed Cyclization of Other Types of Reaction Substrates.** These successes prompted us to apply the present protocol to the cyclization of other substrates having a carboxylic acid and an amide group (Scheme 3). Thus, methyl 2-iodobenzoate was initially subjected to the Sonogashira coupling with phenylacetylene, followed by hydration under basic conditions

(21) When the intramolecular cyclization of **3f** ran with 1 equiv of InBr<sub>3</sub>, the corresponding 7-aza-indole derivative **4f** was obtained in an 18% yield, due to a decline in the nucleophilicity of the tethered amino group by the coordination of the indium catalyst.

## SCHEME 2



## SCHEME 3



to produce the corresponding carboxylic acid **7** in a good yield. Then, treatment of **7** with a catalytic amount of InBr<sub>3</sub> underwent selectively intramolecular 6-*endodig* cyclization, producing the isocoumarin derivative **8** in a quantitative yield. Moreover, the substrate **7** was converted with benzylamine to the corresponding amide **9**. Similarly, when the cyclization of **9** was carried out under optimal conditions, the cyclic amide **10** via 6-*endodig* cyclization was obtained in a 54% yield. Thus, it was found that our group's catalytic system using InBr<sub>3</sub> accommodated an intramolecular cyclization of other types of arylalkynes.

**In-Catalyzed Intermolecular Dimerization Leading to Quinoline Derivatives.** As described in the introduction, when the reaction was carried out using a substrate with a trimethylsilyl group or without a substituent group on the terminal alkyne under our stated optimal conditions, the desired indole product was not produced. This result showed a sharp contrast to the results of other research groups.<sup>20</sup> Thus, we reinvestigated the scope for the dimerization of the ethynylaniline derivative along with the re-examination of a Lewis acid. Initially, the preparation of 2-ethynylaniline **12** was accomplished via both a standard Sonogashira-coupling reaction of 2-iodoaniline with trimethylsilylacetylene and subsequent deprotection of the TMS group under basic conditions (Scheme 4).<sup>19</sup>

The dimerization of 2-ethynylaniline (**12a**) using a typical Lewis acid and indium (III) halide was then reinvestigated, and the results are summarized in Table 4. As a comparison with

## SCHEME 4

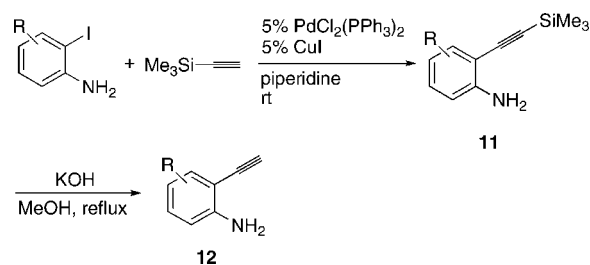


TABLE 4. Examination of Catalyst Effect

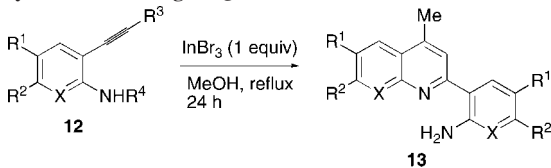
run	LA (equiv)	time (h)	yield (%) <sup>a</sup>
1	Cu(OAc) <sub>2</sub> (0.2)	24	trace
2	InBr <sub>3</sub> (0.05)	36	(58) <sup>b</sup>
3	InBr <sub>3</sub> (0.2)	48	62
4	InBr <sub>3</sub> (1)	24	(89)
5	InCl <sub>3</sub> (1)	24	76
6	InI <sub>3</sub> (1)	24	69
7	In(OTf) <sub>3</sub> (1)	24	71
8	none	24	0 <sup>c</sup>

<sup>a</sup> NMR yield (isolated yield). <sup>b</sup> Average of two runs. <sup>c</sup> Recovery (78%) of **12a**.

results reported by several other groups,<sup>20</sup> our group initially examined the dimerization of ethynylaniline with copper salts (0.2 equiv) under toluene reflux conditions. However, the desired dimerization barely proceeded, resulting in a 95% recovery of the starting material (run 1). On the other hand, increasing the amount of the indium catalyst to 1 equivalent for the ethynylaniline highly improved the yield to an excellent 89% (run 4). Consequently, it was found that a small amount of the indium salt strongly coordinated to the more basic nitrogen atom on the formed quinoline skeleton, resulting in a decline of its catalytic activity. This was strongly supported by the results that the yields of intramolecular cyclization of a substrate having a pyridine ring were rather low (runs 5 and 6 in Table 3). Moreover, like the preparation of indoles, when the reaction was conducted with another indium salt, the corresponding quinoline was obtained in moderate to good yields (runs 5–7).<sup>22</sup>

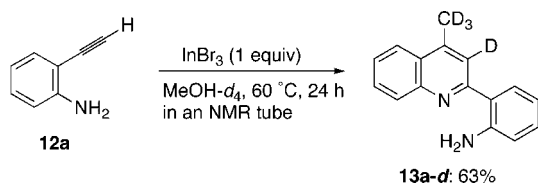
Cyclization reactions of several ethynylaniline derivatives were examined under the above optimal conditions, and the results are shown in Table 5. For example, the use of a substrate having an electron-donating group, such as a methyl and a methoxy group, afforded the desired polysubstituted products **13b–d** in high isolated yields (runs 2–4). In addition, the use of an ethynylaniline derivative containing an electron-withdrawing group, such as a fluoro, a cyano and a nitro group, also gave the corresponding quinoline product **13e–g** (runs 5–7). Surprisingly, when the reaction with a substrate **12h**, having an acetyl group, was conducted under the standard conditions, the dimerization did not proceed, but led to the formation of the acetophenone derivative, which was formed by the hydration of the starting material **12h** (run 8). There is no reasonable explanation for the result. Furthermore, when the substrate having an acetyl group on the amino group or having a nitrogen

(22) When the reaction was ran with 0.2 equiv of InCl<sub>3</sub>, the corresponding quinoline **13a** was obtained in a 20% yield.

**TABLE 5.** In-Catalyzed Intermolecular Dimerization of Ethynylanilines Leading to Quinolines


run	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	X	yield (%) <sup>a</sup>
1	H	H	H	H	CH	(12a) 89 (13a)
2	Me	H	H	H	CH	(12b) 79 (13b)
3	Me	Me	H	H	CH	(12c) 84 (13c)
4	H	MeO	H	H	CH	(12d) 70 (13d)
5	F	H	H	H	CH	(12e) 56 (13e)
6	CN	H	H	H	CH	(12f) 81 (13f)
7	NO <sub>2</sub>	H	H	H	CH	(12g) 80 (13g)
8	Ac	H	H	H	CH	(12h) ND
9	H	H	H	Ac	CH	(12i) ND
10	Me	H	H	H	N	(12j) ND
11	H	H	Me <sub>3</sub> Si	H	CH	(11a) 50 (13a)
12	Me	H	Me <sub>3</sub> Si	H	CH	(11b) 42 (13b)

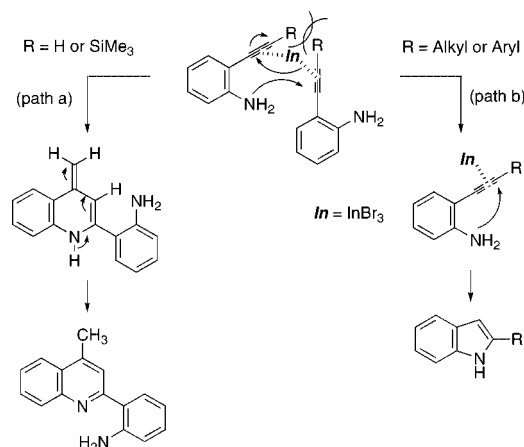
<sup>a</sup> Isolated yield.

**SCHEME 5**

atom embedded in the benzene ring was used, it did not undergo the desired dimerization. The result was a byproduct, which was decomposed by a similar hydration, and the recovery of the starting material **12i,j** (runs 9 and 10). The result of run 9 in Table 5 clarified that a 2-alkynylaniline, which led to the quinoline skeleton, necessarily needed the underivatized amino group. On the other hand, when the reaction was performed with substrates **11a,b** having a trimethylsilyl group at a terminal C≡C bond in the presence of the indium salt, the corresponding products **13a,b** were produced in 50 and 42% yields (runs 11 and 12). Thus, our group's catalytic system using InBr<sub>3</sub> was successful in undergoing the desired intramolecular dimerization, producing the corresponding multisubstituted quinoline derivatives in moderate to good yields.

**Mechanistic Aspect for Intramolecular Cyclization and Intermolecular Dimerization.** To better understand the reaction pathway for the dimerization, a deuterium-labeling experiment was conducted, and the result is shown in Scheme 5. When the reaction with 2-ethynylaniline (**12a**) was carried out in MeOH-*d*<sub>4</sub> at 60 °C, quinoline **13a-d** with a deuterated 4-methyl group and 3-position was obtained in a 63% yield after purification. Additionally, during the reaction <sup>1</sup>H NMR showed a rapid *in situ* H–D exchange on the terminal carbon of **12a**, and <sup>13</sup>C NMR did not detect the new peaks, which supported formation of some intermediates, such as an alkynylindium.<sup>23</sup> On the basis of the deuterium-labeling results, we present a plausible mechanism for the dimerization as shown in Scheme 6. Reactions using ethynylaniline with no substituent group at the terminal carbon would enable the approach of two molecules of the aniline activated by InBr<sub>3</sub> to lead to the dimerization (path

(23) During the dimerization, <sup>13</sup>C NMR observed two peaks (81.1 and 83.5 ppm) of the alkyne moiety of **12a**.

**SCHEME 6**

a in Scheme 6). Thus, to support our group's expected reaction route via path a, the crossed-dimerization using two different ethynylanilines, **12a** and **12c**, was conducted in MeOH-*d*<sub>4</sub> at 60 °C, and the reaction was monitored with <sup>1</sup>H NMR. Surprisingly, the formation of the desired crossed products was not observed, nor was the formation of the original dimerized products. After 18 h, the reaction mixture led to the decomposition of both starting materials. The results implied the existence of another reaction route for a dimerization of the ethynylaniline. By contrast, in the case of aniline derivatives having an alkyl or aryl group, a steric repulsion at the terminal carbon would retard the approach between two molecules, preferring intramolecular cyclization to dimerization (path b in Scheme 6).

## Conclusion

In summary, we have demonstrated that a class of terminal substituents on the triple bond of an ethynylaniline selectively produces two quite different nitrogen-containing heterocycles. First, in alkyl/aryl groups, the indium-catalyzed *intramolecular cyclization* of the alkynylaniline having the unsubstituted amino group occurs predominately to produce the corresponding multifunctionalized indole derivatives. Second, the use of the substrate with a trimethylsilyl group or with no substituent group on the terminal triple bond leads to the production of the polysubstituted quinoline derivative via the *intermolecular dimerization* of the ethynylaniline. Finally, we also have found that the indium catalytic system can be successfully applied to the intramolecular cyclization of other arylalkyne substrates having a carboxylic acid and an amide group.

## Experimental Section

**General Procedure for the Intramolecular Cyclization of the Arylalkyne.** To a 10 mL reaction flask containing a freshly distilled toluene (2 mL) under argon was added arylalkyne **1**, **3**, **7**, or **9** (0.5 mmol) and InBr<sub>3</sub> (0.025–0.50 mmol). The resulting mixture was refluxed and monitored by GC or TLC until the starting material was consumed. After the usual workup, the crude product was purified by silica gel column chromatography (hexane-AcOEt) to produce the corresponding cycloaddition products in yields as shown in Tables 2 and 3 and Scheme 3.

**2-Hexyl-5-nitroindole (2j):** pale-yellow solids; mp 86–87 °C; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 0.87 (brs, 3H), 1.23–1.37 (m, 6H), 1.70–1.73 (m, 2H), 2.76 (t, 2H, *J* = 8 Hz), 6.36 (s, 1H), 7.30 (d, 1H, *J* = 8.5 Hz), 7.99 (d, 1H, *J* = 8.5 Hz), 8.44 (s, 1H), 8.55 (brs, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 14.0, 22.5, 28.1, 28.7, 28.8,

31.5, 101.5, 110.1, 116.7, 128.2, 128.3, 139.1, 141.6, 143.7; MS (FAB): *m/z* 247 (M<sup>+</sup>+H, 100%); HRMS (FAB): Calcd for C<sub>14</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub>: 247.1447, Found: 247.1443; Anal. Calcd for C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>: C, 68.27; H, 7.37; N, 11.37, Found: C, 68.08; H, 7.76; N, 11.58.

**2-(1-Hydroxybutyl)indole (4d)**: yellow oil; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 0.90 (q, 2H, *J* = 7 Hz), 1.05 (t, 2H, *J* = 7 Hz), 1.50 (brs, 1H), 2.01 (t, 2H, *J* = 7 Hz), 2.93 (t, 2H, *J* = 7 Hz), 5.53 (s, 1H), 6.41 (m, 2H), 6.56 (d, 1H, *J* = 7.5 Hz), 6.84 (d, 1H, *J* = 7.5 Hz), 7.50 (brs, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 25.5, 27.8, 31.9, 62.4, 99.3, 110.4, 119.5, 119.7, 120.8, 128.7, 135.9, 139.7; MS (EI): *m/z* 189 (M<sup>+</sup>, 100%); HRMS (EI): Calcd for C<sub>12</sub>H<sub>15</sub>NO: 189.1154, Found: 189.1151.

**1,3,5-(2-Indolyl)benzene (6)**: colorless solids; mp >250 °C; <sup>1</sup>H NMR (500 MHz, *d*<sub>6</sub>-DMSO) δ 7.05 (t, 3H, *J* = 7.5 Hz), 7.15 (m, 6H), 7.47 (d, 3H, *J* = 7.5 Hz), 7.62 (d, 3H, *J* = 7.5 Hz), 8.33 (s, 3H), 11.68 (br s, 3H); <sup>13</sup>C NMR (125 MHz, *d*<sub>6</sub>-DMSO) δ 98.9 (d, *J* = 4.8 Hz), 110.8 (d, *J* = 6.8 Hz), 119.0, 119.7, 119.9, 121.4, 128.0 (d, *J* = 4.8 Hz), 132.8 (d, *J* = 6.8 Hz), 136.5 (d, *J* = 19 Hz), 136.8 (d, *J* = 19 Hz); MS (FAB): *m/z* 424 (M<sup>+</sup>+H, 25%); HRMS (FAB): Calcd for C<sub>30</sub>H<sub>22</sub>N<sub>3</sub>: 424.1814, Found: 424.1819.

**General Procedure for the Intermolecular Dimerization of Ethynylanilines.** To a 10 mL reaction flask under argon containing freshly distilled methanol (0.6 mL) was added 2-(ethynyl)aniline **12** (0.600 mmol) and InBr<sub>3</sub> (0.600 mmol). The resulting mixture was refluxed and monitored by TLC until the starting material had been consumed. After the usual workup, the crude product was

purified by silica gel column chromatography (hexane/AcOEt = 7:3) to produce the polysubstituted quinoline **13** (yields are collected in Table 5).

**2-(7-Methoxy-4-methyl-2-quinoliny)-5-methoxyaniline (13d)**: yellow needles; mp 123.5–124.0 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 2.66 (s, 3H), 3.81 (s, 3H), 3.94 (s, 3H), 6.28 (d, 1H, *J* = 2.4 Hz), 6.32 (brs, 2H), 6.38 (dd, 1H, *J* = 9 Hz, 2.4 Hz), 7.13 (dd, 1H, *J* = 9 Hz, 2.4 Hz) 7.32 (d, 1H, *J* = 2.4 Hz), 7.45 (s, 1H), 7.62 (d, 1H, *J* = 9 Hz), 7.82 (d, 1H, *J* = 9 Hz); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 18.9, 55.1, 55.4, 101.2, 104.1, 107.4, 115.2, 117.9, 118.7, 121.1, 124.6, 131.0, 144.2, 148.4, 149.1, 159.1, 160.4, 161.2; MS (FAB): *m/z* 295 (M<sup>+</sup>+H, 100%); HRMS (FAB): Calcd for C<sub>18</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub>: 295.1446, Found: 295.1458.

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**Supporting Information Available:** Detailed procedures and spectroscopic data for novel compounds. Copies of <sup>1</sup>H NMR of novel compounds prepared are available. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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