

# Formal [4 + 2] Reaction between 1,3-Diynes and Pyrroles: Gold(I)-Catalyzed Indole Synthesis via Double Hydroarylation

Yuka Matsuda, Saori Naoe, Shinya Oishi, Nobutaka Fujii,\* and Hiroaki Ohno\*

**Abstract:** Indole synthesis via a gold(I)-catalyzed intermolecular formal [4 + 2] reaction between 1,3-diynes and pyrroles has been developed. This reaction involves the hydroarylation of 1,3-diynes with pyrroles followed by an intramolecular hydroarylation to give the 4,7-disubstituted indoles. This reaction can also be applied to the synthesis of carbazoles when indoles are used as the nucleophiles instead of pyrroles.

The indole scaffold is a significant structural motif that can be found in a large number of alkaloids, as well as several other bioactive compounds, and a wide range of synthetic methods have been developed for the construction of this core structure.<sup>[1,2]</sup> According to the classification system proposed by Taber et al.,<sup>[2a]</sup> the majority of the traditional synthetic approaches to indoles are based on the construction of the pyrrole ring on an existing benzene ring (Figure 1, Types 1–7). In contrast, very few indole syntheses have been reported to proceed via a [4 + 2]-type reaction (classified as Type 8),<sup>[3]</sup> including the hetero Diels-Alder (DA) reaction of *N*-methylpyrroles (Scheme 1, eq 1)<sup>[4]</sup> and the thermal DA reaction of *N*-tosylpyrroles (eq 2).<sup>[5]</sup> The application of these reactions, however, has been limited because of their requirement for highly activated substrates such as dicyanopyridazine, Danishefsky's diene, and nitrated pyrroles. A related transformation involving the Ru-catalyzed annulation of pyrroles has been developed, but this process requires pent-1-en-4-yn-3-ol derivatives as the C4 synthon (eq 3).<sup>[6]</sup>

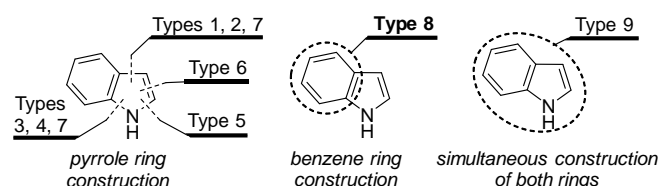
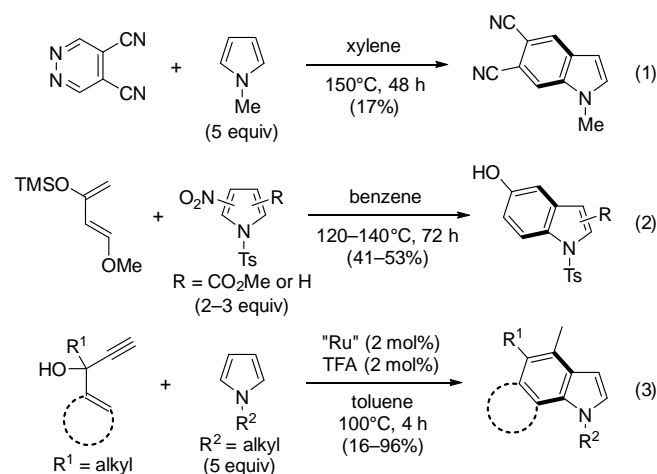


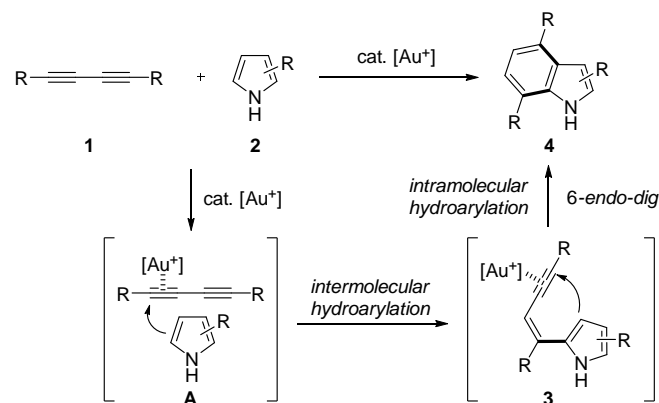
Figure 1. Classification of indole syntheses (Taber et al., 2011)<sup>2a</sup>

Compared with isolated alkynes,<sup>[7,8]</sup> the use of gold catalysis with conjugated diynes,<sup>[9,10]</sup> especially for intermolecular reactions, stands at the very beginning. We designed a new type 8 indole synthesis based on the gold(I)-catalyzed intermolecular

formal [4 + 2] reaction between 1,3-diynes and pyrroles, which could be used to provide convenient access to 4,7-disubstituted indoles. Although numerous 4,7-disubstituted indoles have been reported to show interesting biological activities,<sup>[11]</sup> the existing synthetic methods suffer from multi-step synthesis, low availability of the substrates, and/or limited substrate scope.<sup>[12,13]</sup> It was envisaged that the intermolecular hydroarylation of 1,3-diyne **1** with pyrrole **2** would proceed to give enyne-type intermediate **3**,<sup>[14]</sup> which would undergo an intramolecular 6-*endo-dig* hydroarylation to afford 4,7-disubstituted indole **4** (Scheme 2). Herein, we report a gold(I)-catalyzed intermolecular [4 + 2]-type reaction for the direct synthesis of 4,7-disubstituted indoles using readily available 1,3-diynes and pyrroles. Furthermore, this reaction provided facile access to 1,4-disubstituted carbazoles when *N*-substituted indoles were used as the nucleophile instead of pyrroles.



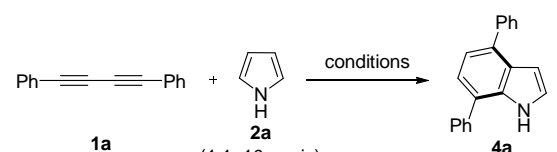
Scheme 1. Indole syntheses via an intermolecular [4 + 2]-type reaction.<sup>[4–6]</sup>



Scheme 2. Our concept: gold(I)-catalyzed [4 + 2]-type indole synthesis via double hydroarylation.

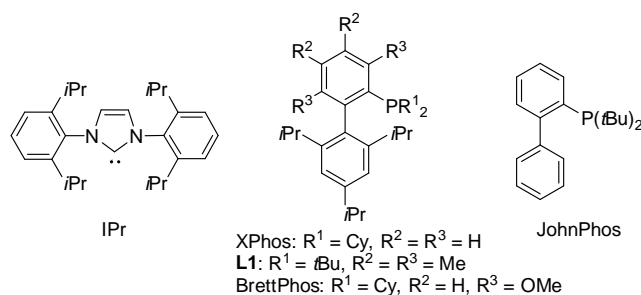
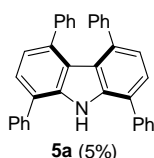
[a] Y. Matsuda, S. Naoe, Dr. S. Oishi, Prof. Dr. N. Fujii, Prof. Dr. H. Ohno  
Graduate School of Pharmaceutical Sciences  
Kyoto University  
Sakyo-ku, Kyoto 606-8501 (Japan)  
E-mail: hohno@pharm.kyoto-u.ac.jp; nfujii@pharm.kyoto-u.ac.jp

Supporting information for this article is available on the WWW under <http://www.angewandte.org> or from the author.

**Table 1.** Optimization of the reaction conditions.<sup>[a]</sup>


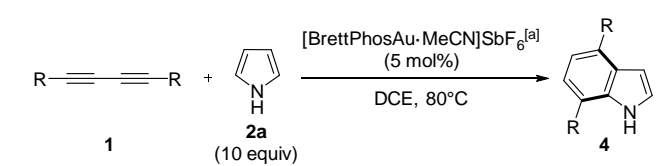
Entry	Catalyst [mol%]	Solvent	t [h]	Yield [%] <sup>[b]</sup>
1	IPrAuCl/AgNTf <sub>2</sub> [10]	toluene	24	22 <sup>[c]</sup>
2	Ph <sub>3</sub> PAuCl/AgNTf <sub>2</sub> [10]	toluene	24	trace
3	JohnPhosAuCl/AgNTf <sub>2</sub> [10]	toluene	24	26 <sup>[c]</sup>
4	XPhosAuCl/AgNTf <sub>2</sub> [10]	toluene	24	32 <sup>[c]</sup>
5	L1AuCl/AgNTf <sub>2</sub> [10]	toluene	24	41
6	BrettPhosAuCl/AgNTf <sub>2</sub> [10]	toluene	24	56
7	BrettPhosAuCl/AgOTf [10]	toluene	24	32
8	BrettPhosAuCl/AgBF <sub>4</sub> [10]	toluene	24	37
9	BrettPhosAuCl/AgPF <sub>6</sub> [10]	toluene	24	trace
10	BrettPhosAuCl/AgSbF <sub>6</sub> [10]	toluene	7.5	57
11	[BrettPhosAu-MeCN]SbF <sub>6</sub> <sup>[d]</sup> [5]	toluene	12	50
12	[BrettPhosAu-MeCN]SbF <sub>6</sub> <sup>[d]</sup> [5]	MeCN	15	41
13	[BrettPhosAu-MeCN]SbF <sub>6</sub> <sup>[d]</sup> [5]	EtOH	15	51
14	<b>[BrettPhosAu-MeCN]SbF<sub>6</sub><sup>[d]</sup> [5]</b>	<b>DCE</b>	<b>12</b>	<b>66</b>
15 <sup>[e]</sup>	[BrettPhosAu-MeCN]SbF <sub>6</sub> <sup>[d]</sup> [5]	DCE	12	59
16 <sup>[f]</sup>	[BrettPhosAu-MeCN]SbF <sub>6</sub> <sup>[d]</sup> [5]	DCE	15	43 <sup>[g]</sup>

[a] Unless otherwise noted, the reactions were conducted using 10 equiv of **2a** at 80°C. [b] Isolated yields. [c] Containing small amounts of impurities. [d] Prepared by mixing BrettPhosAuCl and AgSbF<sub>6</sub> in MeCN and CH<sub>2</sub>Cl<sub>2</sub> followed by filtration. [e] Using 5 equiv of **2a**. [f] Using 1.1 equiv of **2a**. [g] Carbazole **5a** was produced in 5% yield.



The gold-catalyzed reaction of 1,3-diyne **1a** with pyrrole **2a** was selected as a model reaction, and this reaction was subjected to a series of screening experiments to identify the optimum conditions for the transformation (Table 1). The treatment of a mixture of **1a** and **2a** (10 equiv) with 10 mol% of

IPrAuCl and AgNTf<sub>2</sub> in toluene at 80°C gave the desired product **4a** in 22% yield (entry 1). Several phosphine ligands were tested in the reaction (entries 2–6) and BrettPhosAuCl was identified as the optimum catalyst for the reaction, with the desired product **4a** being formed in 56% yield (entry 6). Various silver salts were tested in the reactions (entries 6–10), and AgSbF<sub>6</sub> afforded the best results in terms of the reaction time and yield (entry 10). To simplify the protocol and avoid any issues associated with the use of a hygroscopic silver salt, we used the gold complex [BrettPhosAu-MeCN]SbF<sub>6</sub>,<sup>[15]</sup> which was prepared in advance. A series of different solvents were then screened in the reaction with 5 mol% loading of the catalyst, and the use of 1,2-dichloroethane (DCE) led to an increase in the yield of **4a** to 66% (entry 14). Finally, we examined the effect of the reactant stoichiometry. As the number of equivalents of the pyrrole decreased (e.g., 10, 5, and 1.1 equiv), so too did the yield of **4a** decreased (entries 14–16). This reduction in the yield was attributed in part to a competition between pyrrole **2a** and indole **4a** in terms of their ability to behave as nucleophiles towards **1a**. It is noteworthy that a small amount of carbazole **5a** was produced as an over-reaction product from the nucleophilic addition of **4a** to **1a** (entry 16).

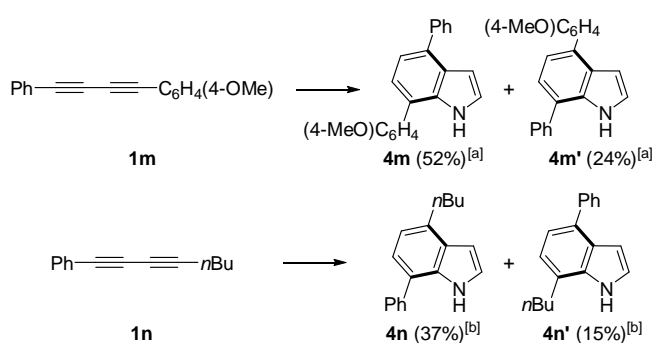
**Table 2.** Reaction of various symmetrical 1,3-diynes.


Entry	Substrate	R	t [h]	Yield [%] <sup>[b]</sup>
1	<b>1a</b>	Ph	12	66
2	<b>1b</b>	C <sub>6</sub> H <sub>4</sub> (4-OMe)	4	85
3	<b>1c</b>	C <sub>6</sub> H <sub>4</sub> (4-Cl)	18	57
4	<b>1d</b>	C <sub>6</sub> H <sub>4</sub> (4-CN)	24	<18 <sup>c</sup>
5	<b>1e</b>	C <sub>6</sub> H <sub>4</sub> (4-CO <sub>2</sub> Me)	24	<26 <sup>c</sup>
6	<b>1f</b>	C <sub>6</sub> H <sub>4</sub> (4-Me)	7	71
7	<b>1g</b>	C <sub>6</sub> H <sub>4</sub> (3-Me)	9	63
8	<b>1h</b>	C <sub>6</sub> H <sub>4</sub> (2-Me)	12	80
9	<b>1i</b>	<i>n</i> Bu	24	56
10 <sup>d</sup>	<b>1j</b>	Cy	24	35
11	<b>1k</b>	2-thienyl	3	62
12	<b>1l</b>	3-thienyl	5	77

[a] Prepared by mixing BrettPhosAuCl and AgSbF<sub>6</sub> in MeCN and CH<sub>2</sub>Cl<sub>2</sub> followed by filtration. [b] Isolated yields. [c] Containing small amounts of impurities. [d] Using 10 mol% of the catalyst.

We proceeded to investigate the scope of this indole synthesis under the optimized conditions (Table 1, entry 14) using a variety of symmetrical 1,3-diynes **1b–l** (Table 2). The diaryl-substituted 1,3-diyne **1b** bearing an electron-donating methoxy group reacted smoothly to afford the corresponding product **4b** in 85% yield (entry 2). Although the chlorinated derivative **1c** showed sufficient reactivity (57%, entry 3), 1,3-diynes bearing a cyano- or methoxycarbonyl substituted diaryl group (i.e., **1d** and **1e**) gave complex mixtures including low yields of **4d** and **4e**, respectively (<18–26%, entries 4 and 5). The position of the substituent in the reactions involving the tolyl derivatives **1f–h** had a moderate impact on the yield of the indole products (63–80%, entries 6–8). Although aliphatic 1,3-diynes such as dibutyl derivative **1i** were well tolerated under the optimized conditions (56%, entry 9), the more bulky dicyclohexyl derivative **1j** gave a much lower yield (35%, entry 10), even when the catalyst loading was increased to 10 mol%. Pleasingly, the dithienyl derivatives **1k** and **1l** reacted smoothly to give the corresponding indoles **4k** and **4l** in good yields (entries 11 and 12). These observations imply that the electron-rich diaryldiynes have higher reactivity than electron-deficient and sterically congested ones toward the indole formation.

We then applied the reaction to unsymmetrical 1,3-diynes (Scheme 3). The reaction of diaryldiyne **1m** gave indole **4m** and its regioisomer **4m'** in 52 and 24% yields, respectively. A similar result was also obtained using diyne **1n** bearing phenyl and *n*-butyl groups, which gave **4n** and the corresponding regioisomer **4n'** in 37 and 15% yields. The major products **4m** and **4n** were most likely formed as a consequence of the first intermolecular hydroarylation occurring at the more electron-rich triple bond of the diyne, which was directly attached to an anisyl or phenyl group. It was assumed that the difficulty associated with controlling the regioselectivity of the first hydroarylation with pyrrole resulted from the conjugated diyne system, with the electronic effects of the terminal substituent(s) extending beyond the proximal alkyne to the distal position.



**Scheme 3.** Reaction of unsymmetrical 1,3-diynes. Reaction conditions: **1** (1 equiv), **2a** (10 equiv) and [BrettPhosAu-MeCN]SbF<sub>6</sub> (5 mol%), DCE, 80°C, 8 h (for **1m**) or 21 h (for **1n**). [a] Determined from the combined isolated yields by <sup>1</sup>H NMR. [b] Isolated yields.

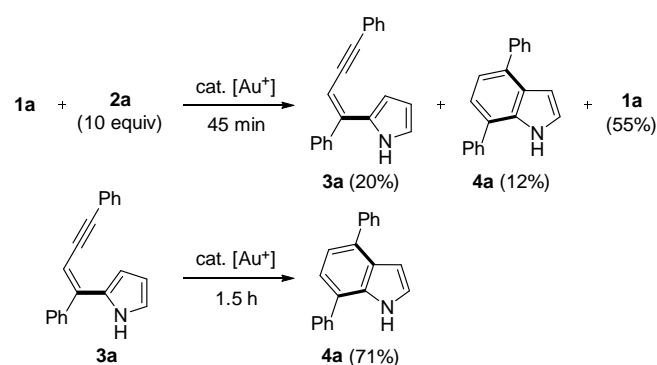
We conducted further substrate scope on this reaction using methyl-substituted pyrroles **2b–d** as shown in Table 3. *N*-methylpyrrole **2b** gave the desired product **4o** in 33% yield along

with other unidentified byproducts (entry 2). Under the above optimized conditions, methyl-substituted pyrroles **2c** and **2d** were converted to the corresponding indoles **4p** and **4q** in low yields (41 and 11%, respectively) with a recovery of the starting material **1a** (entries 3 and 5). Microwave irradiation slightly contributed to improving the yield of **4q** (entry 6). From these investigations, this reaction has a limitation in the synthesis of 4,7-disubstituted indoles bearing pyrrole ring substitution(s). However, this will be able to be overcome by sufficient reactivity of indoles at the pyrrole ring moiety.

**Table 3.** Reaction of **1a** with substituted pyrroles.

Entry	Pyrrole [equiv]	R	T [°C]	t [h]	Product	% Yield <sup>[b]</sup> [Recovery]
1	<b>2a</b> [10]	H	80	12	<b>4a</b>	66
2	<b>2b</b> [10]	1-Me	80	24	<b>4o</b>	33
3	<b>2c</b> [5]	2-Me	80	24	<b>4p</b>	41 [25]
4	<b>2c</b> [5]	2-Me	130 <sup>[c]</sup>	0.5	<b>4p</b>	31 [21]
5	<b>2d</b> [5]	3-Me	80	24	<b>4q</b>	11 [77]
6	<b>2d</b> [5]	3-Me	130 <sup>[c]</sup>	0.5	<b>4q</b>	25 [50]

[a] Prepared by mixing BrettPhosAuCl and AgSbF<sub>6</sub> in MeCN and CH<sub>2</sub>Cl<sub>2</sub> followed by filtration. [b] Isolated yields. [c] Microwave irradiation was used.



**Scheme 4.** Isolation and cyclization of intermediate **3a**. Reaction conditions: [BrettPhosAu-MeCN]SbF<sub>6</sub> (5 mol%), DCE, 80°C.

To develop a deeper understanding of the mechanism, the reaction of **1a** and **2a** was terminated before it reached completion (Scheme 4). Along with the recovered starting material **1a** (55%), enyne-substituted pyrrole **3a** (20%) and the indole **4a** (12%) were isolated from the reaction mixture. As expected, exposure of **3a** to the optimum reaction conditions for

1.5 h led to its complete conversion to the corresponding indole **4a** in 71% yield. This result strongly supported the occurrence of a stepwise double hydroarylation pathway, where the first intermolecular hydroarylation of the 1,3-diyne occurred at the 2-position of the pyrrole (Scheme 2).

**Table 4.** Direct Carbazole Synthesis.

Entry	Substrate	R <sup>1</sup>	R <sup>2</sup>	t [h]	% Yield <sup>[b]</sup> [Recovery]
1	<b>6a</b>	H	H	24	17 [72]
2 <sup>[c]</sup>	<b>6a</b>	H	H	24	50 [22]
3	<b>6b</b>	H	OMe	24	15 [72]
4	<b>6c</b>	H	CO <sub>2</sub> Me	24	23 [57]
5	<b>6d</b>	Me	H	12	57
6	<b>6e</b>	Me	OMe	10	70
7	<b>6f</b>	Me	CO <sub>2</sub> Me	24	45
8	<b>6g</b>	Bn	H	21	78
9	<b>6h</b>	PMB	H	21	54
10	<b>6i</b>	Allyl	H	24	56

[a] Prepared by mixing BrettPhosAuCl and AgSbF<sub>6</sub> in MeCN and CH<sub>2</sub>Cl<sub>2</sub> followed by filtration. [b] Isolated yields. [c] Using 20 mol% of the catalyst.

The development of a reliable synthetic methodology for the construction of carbazoles bearing multiple functionalities in a single step is highly desirable because carbazole-containing derivatives possess a broad range of biological properties, including antibacterial, anti-inflammatory, and antitumor activities.<sup>[8a,16,17]</sup> Carbazoles also exhibit interesting properties as organic materials, such as hole-transporting, photoconductive, and photorefractive effects. Finally, we extended our [4 + 2] type indole formation to the synthesis of carbazoles. We anticipated that indoles would be less reactive as nucleophiles in this transformation than pyrroles because only trace amounts of the corresponding carbazoles, if any, were obtained as the over-reaction products from the reactions of diynes **1** with pyrrole **2a**. For example, the reaction of **1a** with 1.1 equiv of **2a** gave the corresponding carbazole product in only 5% yield (Table 1, entry 16). As anticipated, the reactions of *N*-unsubstituted indoles **6a–c** were sluggish, with the desired products **7a–c** being formed in only 15–23% yields (Table 4, entries 1, 3 and 4). It is noteworthy that large amounts of the starting material **1a** were recovered in these cases. Increasing the loading of catalyst to 20 mol% led to a small improvement in the yield of **7a** to 50% (entry 2). In

contrast, *N*-methylindoles **6d–f** reacted efficiently in the presence of 5 mol% of the catalyst to give **7d–f** in moderate yields (entries 5–7). Similarly, other *N*-substituted indoles **6g–i** bearing a benzyl, *para*-methoxybenzyl (PMB), or allyl group on their nitrogen reacted effectively to give the corresponding *N*-substituted carbazoles **7g–i** in acceptable yields (entries 8–10). Based on these results, it appeared likely that the proton on the indole nitrogen was having an adverse impact on the formation of carbazoles from indoles and that a protecting group was therefore necessary to allow indoles to be used as substrates in this reaction.

In summary, we have developed a new method for the synthesis of 4,7-disubstituted indoles based on the gold(I)-catalyzed intermolecular formal [4 + 2] reaction between 1,3-diynes and pyrroles. The use of *N*-substituted indoles as the nucleophile allowed for the direct synthesis of 1,4-disubstituted carbazoles. Studies directed towards the application of this method to the total synthesis of biologically active indole alkaloids are currently underway in our laboratory.

## Acknowledgements

This work was supported by a Grant-in-Aid for the Encouragement of Young Scientists (A), as well as Platform for Drug Design, Discovery, and Development from the Ministry of Education, Culture, Sports, Science and Technology, Japan. S.N. would like to express her gratitude for Research Fellowships from the Japan Society for the Promotion of Science for Young Scientists.

**Keywords:** indole • cascade reaction • gold catalysis • hydroarylation • carbazole

- [1] For recent reviews on indole alkaloids, see: a) A. J. Kochanowska-Karamyan, M. T. Hamann, *Chem. Rev.* **2010**, *110*, 4489–4497; b) M. Ishikura, T. Abe, T. Choshi, S. Hibino, *Nat. Prod. Rep.* **2013**, *30*, 694–752.
- [2] For recent reviews on indole synthesis, see: a) D. F. Taber, P. K. Tirunahari, *Tetrahedron* **2011**, *67*, 7195–7210; b) S. Cacchi, G. Fabrizi, A. Goggiamani, *Org. Biomol. Chem.* **2011**, *9*, 641–652; c) R. Vicente, *Org. Biomol. Chem.* **2011**, *9*, 6469–6480; d) M. Inman, C. J. Moody, *Chem. Sci.* **2013**, *4*, 29–41.
- [3] For stepwise indole syntheses of Type 8, see: a) J. Moskal, A. M. van Leussen, *J. Org. Chem.* **1986**, *51*, 4131–4139; b) M. Iwasaki, Y. Kobayashi, J.-P. Li, H. Matsuzaka, Y. Ishii, M. Hidai, *J. Org. Chem.* **1991**, *56*, 1922–1927; c) H. Ishibashi, T. Tabata, K. Hanaoka, H. Iriyama, S. Akamatsu, M. Ikeda, *Tetrahedron Lett.* **1993**, *34*, 489–492; d) A. R. Katritzky, S. Ledoux, S. K. Nair, *J. Org. Chem.* **2003**, *68*, 5728–5730; e) M. Kim, E. Vedejs, *J. Org. Chem.* **2004**, *69*, 6945–6948; f) N. Asao, H. Aikawa, *J. Org. Chem.* **2006**, *71*, 5249–5253; g) J. Zhao, C. O. Hughes, F. D. Toste, *J. Am. Chem. Soc.* **2006**, *128*, 7436–7437; h) X.-Y. Liu, C.-M. Che, *Angew. Chem.* **2009**, *121*, 2403–2407; *Angew. Chem. Int. Ed.* **2009**, *48*, 2367–2371.
- [4] a) R. Nesi, D. Giomi, S. Turchi, A. Falai, *J. Chem. Soc., Chem. Commun.* **1995**, 2201–2202; b) D. Giomi, M. Cecchi, *Tetrahedron* **2002**, *58*, 8067–8071.
- [5] C. Della Rosa, M. Kneeteman, P. Mancini, *Tetrahedron Lett.* **2007**, *48*, 1435–1438.
- [6] N. Thies, C. G. Hrib, E. Haak, *Chem. Eur. J.* **2012**, *18*, 6302–6308.

- 
- [7] For recent reviews on gold catalysis, see: a) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180–3211; b) D. J. Gorin, F. D. Toste, *Nature* **2007**, *446*, 395–403; c) H. C. Shen, *Tetrahedron* **2008**, *64*, 3885–3903; d) H. Ohno, *Isr. J. Chem.* **2013**, *53*, 869–882; e) G. Abbiati, F. Marinelli, E. Rossi, A. Arcadi, *Isr. J. Chem.* **2013**, *53*, 856–868.
- [8] For our recent studies, see: a) K. Hirano, Y. Inaba, N. Takahashi, M. Shimano, S. Oishi, N. Fujii, H. Ohno, *J. Org. Chem.* **2011**, *76*, 1212–1227; b) K. Hirano, Y. Inaba, K. Takasu, S. Oishi, Y. Takemoto, N. Fujii, H. Ohno, *J. Org. Chem.* **2011**, *76*, 9068–9080; c) S. Naoe, Y. Suzuki, K. Hirano, Y. Inaba, S. Oishi, N. Fujii, H. Ohno, *J. Org. Chem.* **2012**, *77*, 4907–4916; d) H. Chiba, S. Oishi, N. Fujii, H. Ohno, *Angew. Chem.* **2012**, *124*, 9303–9306; *Angew. Chem. Int. Ed.* **2012**, *51*, 9169–9172; e) Y. Suzuki, S. Naoe, S. Oishi, N. Fujii, H. Ohno, *Org. Lett.* **2012**, *14*, 326–329; f) Y. Tokimizu, S. Oishi, N. Fujii, H. Ohno, *Org. Lett.* **2014**, *16*, 3138–3141.
- [9] For the pioneering works on intermolecular reaction with 1,3-dynes, see: a) D. J. Gorin, P. Dubé, F. D. Toste, *J. Am. Chem. Soc.* **2006**, *128*, 14480–14481; b) V. Lavallo, G. D. Frey, B. Donnadieu, M. Soleilhavoup, G. Bertrand, *Angew. Chem.* **2008**, *120*, 5302–5306; *Angew. Chem. Int. Ed.* **2008**, *47*, 5224–5228; c) S. Kramer, J. L. H. Madsen, M. Rottländer, T. Skrydstrup, *Org. Lett.* **2010**, *12*, 2758–2761.
- [10] For intramolecular reactions with 1,3-dynes, see: a) J. Mo, D. Eom, E. Lee, P. H. Lee, *Org. Lett.* **2012**, *14*, 3684–3687; b) P. P. Sharp, M. G. Banwell, J. Renner, K. Lohmann, A. C. Willis, *Org. Lett.* **2013**, *15*, 2616–2619.
- [11] For biologically active 4,7-disubstituted indoles, see: a) G. Groszek, A. Nowak-Król, T. Wdowik, D. Świerczyński, M. Bednarski, M. Otto, M. Walczak, B. Filipek, *Eur. J. Med. Chem.* **2009**, *44*, 5103–5111; b) A. Paulsen, M. Williams, H. M. Nagaraj, A. D. William, H. Wang, C. K. Soh, Z. C. Xiong, B. Dymock, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 1009–1013; c) K. M. Foote, K. Blades, A. Cronin, S. Fillery, S. S. Guichard, L. Hassall, I. Hickson, X. Jacq, P. J. Jewsbury, T. M. McGuire, J. W. M. Nissink, R. Odedra, K. Page, P. Perkins, A. Suleman, K. Tam, P. Thommes, R. Broadhurst, C. Wood, *J. Med. Chem.* **2013**, *56*, 2125–2138.
- [12] For Type 8 synthesis of 4,7-disubstituted indoles, see: a) M. Abid, A. Spaeth, B. Török, *Adv. Synth. Catal.* **2006**, *348*, 2191–2196; b) A. Palmieri, S. Gabrielli, D. Lanari, L. Vaccaro, R. Ballini, *Adv. Synth. Catal.* **2011**, *353*, 1425–1428; c) E. Nojman, L. Latos-Grażyński, L. Szterenber, *Eur. Org. Chem.* **2012**, 4115–4122; d) H. Cho, F. Török, B. Török, *Green Chem.* **2014**, *16*, 3623–3634.
- [13] For other stepwise syntheses of 4,7-disubstituted indoles, see: a) K. R. Rathikrishnan, V. K. Indirapriyadarshini, S. Ramakrishna, R. Murugan, *Tetrahedron* **2011**, *67*, 4025–4030; b) I. R. M. Tébeka, G. B. Longato, M. V. Craveiro, J. E. de Carvalho, A. L. T. G. Ruiz, L. F. Silva, Jr., *Chem. Eur. J.* **2012**, *18*, 16890–16901; c) W. Liu, H. J. Lim, T. V. RajanBabu, *J. Am. Chem. Soc.* **2012**, *134*, 5496–5499; d) C. Clarisse, B. Pelotier, O. Piva, F. Fache, *Chem. Commun.* **2012**, *48*, 157–159.
- [14] We recently reported that pyrrole can be used as a nucleophile in gold-catalyzed reaction of alkynes: see, ref 8c.
- [15] For preparation of related gold complexes, see: C. Obradors, D. Leboeuf, J. Aydin, A. M. Echavarren, *Org. Lett.* **2013**, *15*, 1576–1579.
- [16] For recent reviews, see: a) A. W. Schmidt, K. R. Reddy, H.-J. Knölker, *Chem. Rev.* **2012**, *112*, 3193–3328; b) J. Roy, A. K. Jana, D. Mal, *Tetrahedron* **2012**, *68*, 6099–6121; c) N. Yoshikai, Y. Wei, *Asian J. Org. Chem.* **2013**, *2*, 466–478.
- [17] For our recent studies, see: a) S. Oishi, T. Watanabe, J. Sawada, A. Asai, H. Ohno, N. Fujii, *J. Med. Chem.* **2010**, *53*, 5054–5058; b) T. Takeuchi, S. Oishi, T. Watanabe, H. Ohno, J. Sawada, K. Matsuno, A. Asai, N. Asada, K. Kitaura, N. Fujii, *J. Med. Chem.* **2011**, *54*, 4839–4846.
-