

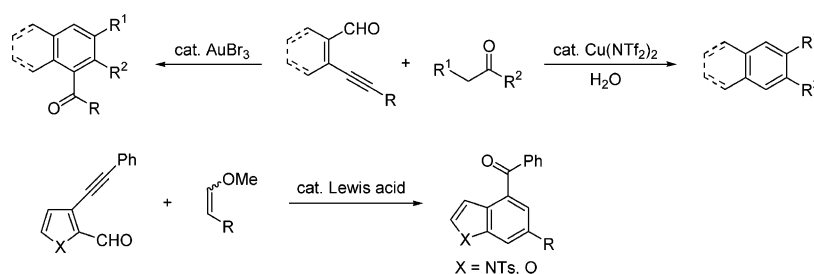
# Lewis Acid-Catalyzed [4 + 2] Benzannulation between Enynal Units and Enols or Enol Ethers: Novel Synthetic Tools for Polysubstituted Aromatic Compounds Including Indole and Benzofuran Derivatives

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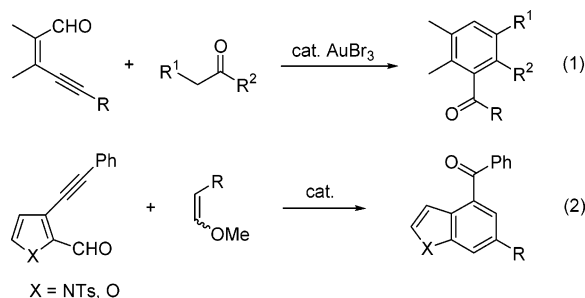


The reaction of enynals **1**, including *o*-(alkynyl)benzaldehydes, and carbonyl compounds **2**, such as aldehydes and ketones, in the presence of a catalytic amount of AuBr<sub>3</sub> in 1,4-dioxane at 100 °C gave the functionalized aromatic compounds **3** in high yields. Similarly, the AuBr<sub>3</sub>-catalyzed reactions of **1** with acetal compounds **5** afforded the corresponding aromatic compounds **3** in good yields. On the other hand, when the reaction was carried out in the presence of a catalytic amount of Cu(NTf<sub>2</sub>)<sub>2</sub> and 1 equiv of H<sub>2</sub>O in (CH<sub>2</sub>Cl)<sub>2</sub> at 100 °C, the decarbonylated naphthalene products **4** were obtained selectively over **3**. Benzofused heteroaromatic compounds, such as indole derivatives **13** and benzofuran derivatives **15**, were also synthesized by using the present benzannulation methodology.

## Introduction

Stereodefined synthesis of polysubstituted aromatic compounds is highly important in modern organic chemistry. Since Reppe's pioneering work on metal-catalyzed benzannulations using [2 + 2 + 2] cyclootrimerization of alkynes,<sup>1</sup> a number of synthetic methods using transition-metal catalysts have been reported.<sup>2</sup> However, efficient synthetic methods are still needed from the viewpoint of atom economy or environmental concern. Recently, we have communicated the novel gold-catalyzed [4 + 2] benzannulation between enynal units, including *o*-(alkynyl)benzaldehydes, and carbonyl compounds, which produces aromatic ketones in good to high yields as shown in eq 1.<sup>3,4</sup> Now, we report the detailed study on this reaction

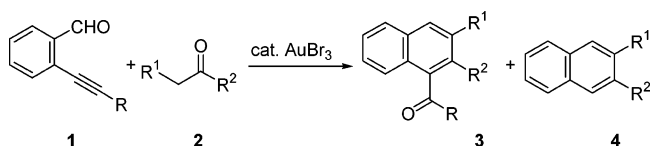
together with a novel synthetic method of benzofused heteroaromatic compounds, such as indole and benzofuran derivatives (eq 2).



## Results and Discussion

**(A) Benzannulation Using Enynal Units and Carbonyl Compounds.** As we previously reported, the [4 + 2] cycloaddition reaction of *o*-(alkynyl)benzaldehydes **1** with various kinds of carbonyl compounds **2** proceeded smoothly in the presence of gold catalyst, leading to naphthyl ketone derivatives **3** together

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 (1) (a) Reppe, W.; Schweckendieck, W. J. *Liebigs Ann. Chem.* **1948**, 560, 104. For references, see: (b) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, 23, 539. (c) Mohler, D. L.; Vollhardt, K. P. C. In *Advances in Strain in Organic Chemistry*; Halton, B., Ed.; JAI Press: London, 1995; Vol. 5, p 121.

**TABLE 1.** AuBr<sub>3</sub>-Catalyzed [4 + 2] Benzannulation between *o*-(Alkynyl)benzaldehydes **1** and Carbonyl Compounds **2**<sup>a</sup>

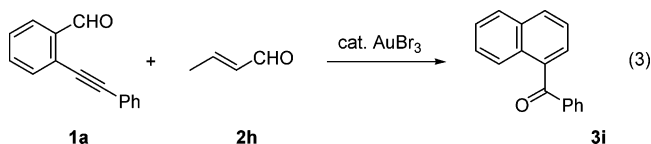
entry	<b>1</b>	R	<b>2</b>	R <sup>1</sup>	R <sup>2</sup>	ratio ( <b>3</b> : <b>4</b> ) <sup>b</sup>	yield (%) <sup>c</sup>	
1	<b>1a</b>	Ph	<b>2a</b>	Ph	H	<b>3a</b> : <b>4a</b>	87:13	90
2 <sup>d,e</sup>	<b>1a</b>	Ph	<b>2b</b>	CH <sub>3</sub>	H	<b>3b</b> : <b>4b</b>	97:3	87
3	<b>1a</b>	Ph	<b>2c</b>	C <sub>5</sub> H <sub>11</sub>	H	<b>3c</b> : <b>4c</b>	99:<1	81
4 <sup>f</sup>	<b>1a</b>	Ph	<b>2d</b>	<sup>i</sup> Pr	H	<b>3d</b> : <b>4d</b>	80:20	81
5 <sup>g</sup>	<b>1a</b>	Ph	<b>2e</b>	-(CH <sub>2</sub> ) <sub>4</sub> -	H	<b>3e</b> : <b>4e</b>	82:18	56
6 <sup>f</sup>	<b>1a</b>	Ph	<b>2f</b>	H	CH <sub>3</sub>	<b>3f</b> : <b>4f</b>	91:9	45
7	<b>1a</b>	Ph	<b>2g</b>	BnO	H	<b>3g</b> : <b>4g</b>	99:<1	45
8 <sup>d</sup>	<b>1b</b>	C <sub>4</sub> H <sub>9</sub>	<b>2b</b>	CH <sub>3</sub>	H	<b>3h</b> : <b>4h</b>	99:<1	71

<sup>a</sup> The reaction was performed using **1** (1 equiv) and **2** (1.2 equiv) in the presence of AuBr<sub>3</sub> (10 mol %) in 1,4-dioxane at 100 °C within 3 h unless otherwise noted. <sup>b</sup> Determined by <sup>1</sup>H NMR. <sup>c</sup> Combined isolated yield. <sup>d</sup> Five equivalents of **2b** were used. <sup>e</sup> The reaction was carried out at 80 °C. <sup>f</sup> The reaction was carried out in the presence of 30 mol % of AuBr<sub>3</sub>. <sup>g</sup> The reaction was carried out in the presence of 20 mol % of AuBr<sub>3</sub>.

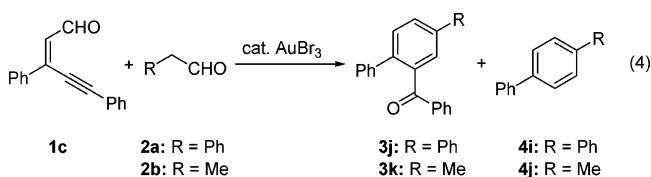
with small amounts of decarbonylated products **4** in good to high yields, and the results are summarized in Table 1.<sup>4,5</sup> The reaction proceeded well even with the sterically bulky aldehyde, such as 3-methylbutanal **2d**, although an increased amount of catalyst was needed (entry 4). In addition to aldehydes, ketones were also usable as a 2π-system in the present reaction. When **1a** was treated with cyclohexanone **2e**, the corresponding six-membered annulated naphthalene **3e** was obtained in a moderate yield (entry 5). Analogously, the reaction of **1a** with acetone **2f** proceeded to give **3f**, which is a regioisomer of **3b** (entry 6). Not only simple alkyl and aryl substituents can be introduced to the naphthalene skeleton; an alkoxy group can also be introduced to the naphthalene skeleton. The reaction of **1a** with benzyloxyacetaldehyde **2g** gave **3g** as a sole product (entry 7). The benzannulation of **1b**, having butyl group at the terminal position of alkyne, with **2b** gave **3h** in 71% yield (entry 8). In every case, we did not detect the regioisomers of **3**; R<sup>1</sup> was always at the C-3 position and R<sup>2</sup> was always at the C-2 position.

Interestingly, when the reaction of **1a** with crotonaldehyde **2h** was examined, naphthyl phenyl ketone **3i** was obtained in

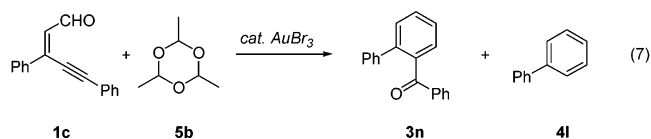
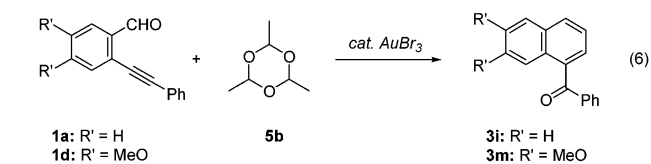
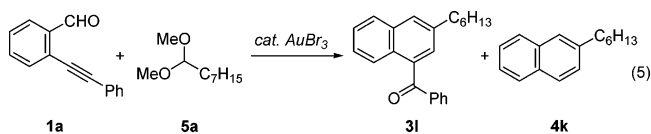
13% yield (eq 3). Probably, acetaldehyde would be produced in situ by the retro-aldol condensation between **2h** and a small amount of water, which might exist in the media. Then, the benzannulation between the resulting acetaldehyde and **1a** would take place to afford **3i**. This result clearly shows that **2h** can be used as a masked acetaldehyde in the [4 + 2] benzannulation, although the chemical yield of **3i** was low.



Not only the benzaldehyde derivatives underwent benzannulation; conjugated enyne aldehydes also underwent benzannulation, leading to polysubstituted benzene derivatives regioselectively. For example, the reaction of **1c** with phenylacetaldehyde **2a** gave terphenyl derivative **3j** and **4i** in 42 and 6%, respectively. When the reaction was carried out using propanal **2b**, **3k** was obtained in 70% together with **4j** in 12% yield (eq 4).



The reaction of **1** with acetal compounds **5**, instead of carbonyl compounds **2**, also proceeded to give a variety of aromatic compounds. Treatment of **1a** with 1,1-dimethoxyoctane **5a** in the presence of gold catalyst gave the corresponding naphthalene derivative **3l** in 27% yield. The chemical yield was improved by addition of water (3 equiv), and **3l** was obtained in 68% yield together with **4k** in 5% yield (eq 5). We also examined the reaction of **1a** and **1d** with paraldehyde **5b**. Even without external addition of water, the corresponding products **3i** and **3m** were obtained in 61 and 52% yields, respectively (eq 6). Furthermore, the reaction between **1c** and **5b** proceeded smoothly to give benzophenone derivative **3n** in 51% yield together with a small amount of **4l** (8%) (eq 7). These results showed that **5b** can work as an acetaldehyde source in the [4 + 2] benzannulation as well as **2h**.

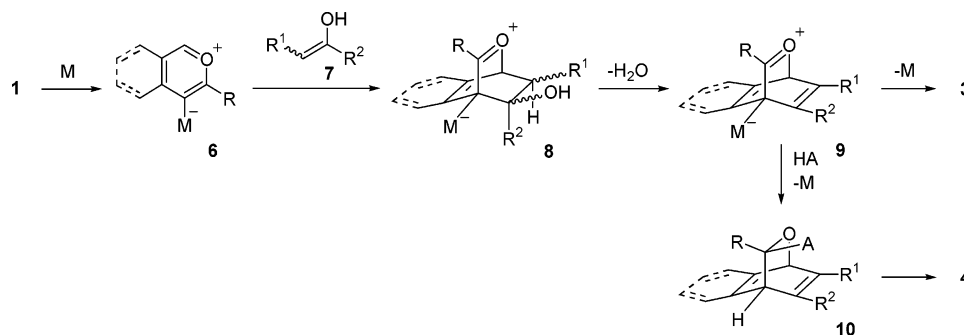


(2) For reviews, see: (a) Kotha, S.; Brahmachary, E.; Lahiri, K. *Eur. J. Org. Chem.* **2005**, 4741. (b) *Modern Arene Chemistry*; Astruc, D., Ed.; Wiley-VCH: Weinheim, 2002. (c) Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901. (d) Gevorgyan, V.; Yamamoto, Y. *J. Organomet. Chem.* **1999**, *576*, 232. (e) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49. (f) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259. (g) Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: Oxford, 1995; Vol. 12, p 741. (h) Schore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, p 1129. (i) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081.

(3) Asao, N.; Aikawa, H.; Yamamoto, Y. *J. Am. Chem. Soc.* **2004**, *126*, 7458.

(4) For reviews on the Au-catalyzed reactions, see: (a) Ma, S.; Yu, S.; Gu, Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 200. (b) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2005**, *44*, 6990. (c) Hoffmann-Röder, A.; Krause, N. *Org. Biomol. Chem.* **2005**, *3*, 387. (d) Arcadi, A.; Di Giuseppe, S. *Curr. Org. Chem.* **2004**, *8*, 795. (e) Hashmi, A. S. K. *Gold Bull.* **2004**, *37*, 51. (f) Hashmi, A. S. K. *Gold Bull.* **2003**, *36*, 3. (g) Dyker, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 4237.

(5) For gold-catalyzed benzannulation, see: (a) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *J. Am. Chem. Soc.* **2000**, *122*, 11553. (b) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *Org. Lett.* **2001**, *3*, 3769. (c) Dankwardt, J. W. *Tetrahedron Lett.* **2001**, *42*, 5809. (d) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *Catal. Today* **2002**, *72*, 19.

SCHEME 1. Plausible Reaction Mechanism of the [4 + 2] Benzannulation between **1** and **2**TABLE 2. Copper-Catalyzed Benzannulation between **1a** and **2b**<sup>a</sup>

entry	Lewis acid	additives	ratio ( <b>3b</b> : <b>4b</b> ) <sup>b</sup>	yield (%) <sup>c</sup>
1	Cu(OTf) <sub>2</sub>	none	60:40	80
2	Cu(OTf) <sub>2</sub>	CF <sub>2</sub> HCO <sub>2</sub> H	48:52	79
3	Cu(OTf) <sub>2</sub>	CF <sub>3</sub> CO <sub>2</sub> H	38:62	66
4	Cu(NTf <sub>2</sub> ) <sub>2</sub>	none	13:87	31
5	Cu(NTf <sub>2</sub> ) <sub>2</sub>	H <sub>2</sub> O	10:90	48

<sup>a</sup> The reaction was performed using **1a** (1 equiv) and **2b** (5 equiv) in the presence of Lewis acid (10 mol %) and additives (1 equiv) in (CH<sub>2</sub>Cl)<sub>2</sub> at 100 °C within 2 h. <sup>b</sup> Determined by <sup>1</sup>H NMR. <sup>c</sup> Combined NMR yield using *p*-xylene as an internal standard.

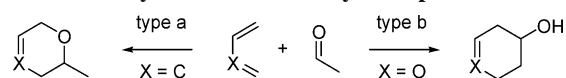
We have reported that the AuX<sub>3</sub>-catalyzed benzannulation between enynal unit **1** and alkynes gives aromatic compounds **3** in high yields.<sup>6</sup> On the other hand, selective formation of the decarbonylated products **4** over **3** was observed by changing the catalyst from AuX<sub>3</sub> to a combination of a catalytic amount of Cu(OTf)<sub>2</sub> and a stoichiometric amount of Brønsted acid.<sup>6b</sup> Therefore, we were interested whether the similar decarbonylation reaction would be possible in the present reaction. We examined the reaction of **1a** with **2b** using the copper catalyst in the presence of Brønsted acid under the several conditions, and results are summarized in Table 2. When the reaction was conducted in the presence of a catalytic amount of Cu(OTf)<sub>2</sub> without Brønsted acid, **3b** was obtained predominantly over **4b** in 80% yield as a combined yield of **3b** and **4b** (entry 1). Optimization experiments revealed that the addition of Brønsted acids, such as CF<sub>2</sub>HCO<sub>2</sub>H and CF<sub>3</sub>CO<sub>2</sub>H, increased the ratio of **4b** against **3b** (entries 2 and 3). Finally, we found that the best selectivity was obtained by using the Cu(NTf<sub>2</sub>)<sub>2</sub>-H<sub>2</sub>O system and **4b** was produced in 43% yield together with a small amount of **3b** (5%) (entry 5).

A plausible mechanism for the present benzannulation is shown in Scheme 1.<sup>3,4,7,8</sup> The coordination of the triple bond of **1** to Lewis acid (M: AuX<sub>3</sub> or Cu(NTf<sub>2</sub>)<sub>2</sub>) enhances the electrophilicity of the alkyne, and the subsequent nucleophilic attack of the carbonyl oxygen to the electron-deficient alkyne would form the ate complex **6**. The reverse electron demand-type Diels-Alder reaction of **6** with the enol **7**, derived from

**2**, followed by dehydration would generate the intermediate **9** through **8**. When the reaction is catalyzed by AuX<sub>3</sub>, the subsequent bond rearrangement would afford the naphthyl ketone derivatives **3** and regenerate AuX<sub>3</sub>. On the other hand, in the Cu(NTf<sub>2</sub>)<sub>2</sub>-HA system, protonolysis of the C-Cu bond of **9** by HA, followed by the attack of A<sup>-</sup> to the carbon of RCO, would produce **10**, which would undergo the retro Diels-Alder reaction to lead the formation of **4**. It is worth mentioning that when the AuX<sub>3</sub>-catalyzed reaction of **1a** with **2b** was carried out in the presence of MS 3A under conditions similar to those mentioned in Table 1, the chemical yield of **3b** was dramatically decreased and only trace amounts of **3b** were obtained. Trace amounts of water, which might exist in the reaction medium, would play an important role for the keto-enol tautomerization between **2b** and **7**.<sup>9,10</sup> The reaction would probably not proceed well without water due to the lack of the generation of enol form **7**.

In the normal electron demand-type Diels-Alder reaction between diene systems and carbonyl compounds, it is well-known that the carbon-oxygen double bond of carbonyl compounds acts as a 2π-system with various 4π-systems as a hetero-Diels-Alder reaction (type a in Scheme 2). However, to the best of our knowledge, the present benzannulation is the first example of the Lewis acid-catalyzed reverse electron demand-type cycloaddition between a 4π-system and an enol derived from an aldehyde and ketone (type b in Scheme 2).<sup>11</sup>

## SCHEME 2. Reaction Type of the Diels-Alder Reaction between Diene Systems and Carbonyl Compounds



## (B) Benzannulation Using Enynal Units and Enol Ethers.

In addition to carbonyl compounds, enol ethers can be used for the present benzannulation reaction.<sup>12-14</sup> The reaction of **1a** with β-methoxystyrene **11a** using AuBr<sub>3</sub> catalyst proceeded, and naphthyl ketone product **3a** was obtained in 42% yield. The chemical yield of **3a** was increased to 84% when the reaction

(6) (a) Asao, N.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12650. (b) Asao, N.; Nogami, T.; Lee, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 10921.

(7) For acid-induced pyrylium salts syntheses by electrophilic cyclizations of *o*-alkynyl(oxo)benzenes, see: (a) Tovar, J. D.; Swager, T. M. *J. Org. Chem.* **1999**, *64*, 6499. (b) Barluenga, J.; Vázquez-Villa, H.; Ballesteros, A.; González, J. M. *J. Am. Chem. Soc.* **2003**, *125*, 9028. (c) Zhu, J.; Germain, A. R.; Porco, J. A., Jr. *Angew. Chem., Int. Ed.* **2004**, *43*, 1239.

(8) Benzo[*c*]pyrylium salts are known to play a dien part in the Diels-Alder reaction with ethyl vinyl ether and azomethines. See: Kuznetsov, E.; Shcherbakova, I. V.; Balaban, A. T. *Adv. Heterocycl. Chem.* **1990**, *50*, 157.

(9) A protic catalyst, which is formed from AuBr<sub>3</sub> in water, might promote the enolization process. See: Dyker, G.; Hildebrandt, D.; Liu, J.; Merz, K. *Angew. Chem., Int. Ed.* **2003**, *42*, 4399.

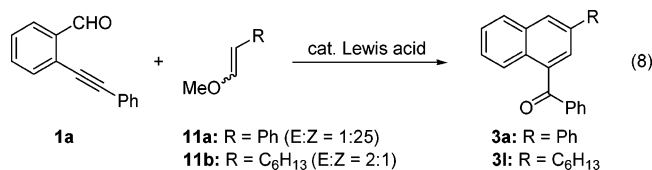
(10) A theoretical study on keto-enol tautomerization was reported. See: Lee, D.; Kim, C. K.; Lee, B.-S.; Lee, I.; Lee, B. C. *J. Comput. Chem.* **1997**, *18*, 56 and references therein.

(11) For example, see: Fringuelli, F.; Taticchi, A. *The Diels-Alder Reaction-Selected Practical Methods*; Wiley: Chichester, 2002.

(12) Asao, N.; Kasahara, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2003**, *42*, 3504.

(13) Pt-catalyzed benzannulation using *ortho*-alkynyl benzoates and vinyl ethers was reported. See: Kusama, H.; Funami, H.; Takaya, J.; Iwasawa, N. *Org. Lett.* **2004**, *6*, 605.

was carried out using  $\text{Cu}(\text{OTf})_2$  instead of  $\text{AuBr}_3$ . The  $\text{Cu}(\text{OTf})_2$ -catalyzed reaction of **1a** with **11b** also proceeded to give **31** in 56% yield (eq 8).



**(C) Construction of Benzofused Heteroaromatic Compounds.** We next turned our attention to the construction of benzofused heteroaromatic compounds by using the present methodology. Although many synthetic methods of indole and benzofuran skeletons are known,<sup>15</sup> little attention has been paid to the approach based on the construction of a benzene ring onto a functionalized pyrrole and furan derivatives.<sup>16</sup> During our research project, Barluenga et al. reported that the iodonium-mediated benzannulation reaction using 3-alkynylpyrrole-2-carboxaldehydes with alkenes (or the corresponding enamines or enol ethers) led to indole derivatives.<sup>17</sup> Benzofuran and benzothiophene derivatives were also prepared in the same way. To develop the catalytic version, we examined the reaction of **12** with enol ether **11** in the presence of several kinds of catalysts, and results are summarized in Table 3. The reaction of **12** with  $\beta$ -methoxystyrene **11a** in the presence of a catalytic amount of  $\text{Cu}(\text{OTf})_2$  gave **13a** in 90% yield (entry 1).  $\text{AuBr}_3$  and  $\text{AgNTf}_2$  were also suitable catalysts (entries 2 and 3). Although the reaction proceeded even with a catalytic amount of TFOH, the chemical yield was low (entry 4). The reaction of **12** with other enol ethers, such as 1-methoxy-1-octene **11b**, butoxyethene **11c**, and 1-methoxycyclohexene **11d**, proceeded to give the corresponding products **13b–d** in good to high yields (entries 5–7).

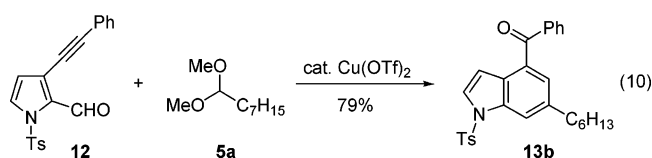
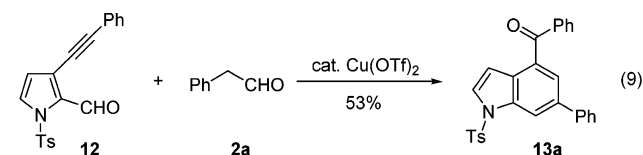
**TABLE 3.** Lewis Acid-Catalyzed Indole Synthesis<sup>a</sup>

entry	<b>11</b>	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	catalyst	<b>13</b>	yield (%) <sup>b</sup>
1	<b>11a</b>	Ph	H	Me	$\text{Cu}(\text{OTf})_2$	<b>13a</b>	90
2	<b>11a</b>	Ph	H	Me	$\text{AuBr}_3$	<b>13a</b>	70
3	<b>11a</b>	Ph	H	Me	$\text{AgNTf}_2$	<b>13a</b>	88
4	<b>11a</b>	Ph	H	Me	TFOH	<b>13a</b>	15
5	<b>11b</b>	$\text{C}_6\text{H}_{13}$	H	Me	$\text{AuBr}_3$	<b>13b</b>	97
6	<b>11c</b>	H	H	$\text{C}_4\text{H}_9$	$\text{AuBr}_3$	<b>13c</b>	83
7	<b>11d</b>	$-(\text{CH}_2)_4-$	Me		$\text{Cu}(\text{OTf})_2$	<b>13d</b>	64

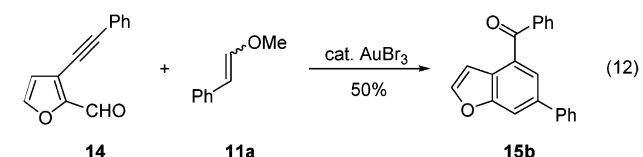
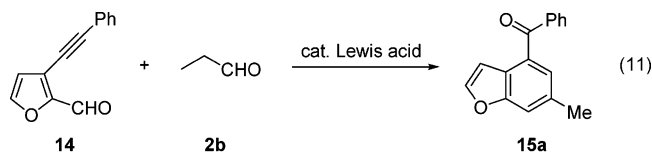
<sup>a</sup> The reaction was performed using **11** and **12** in the presence of Lewis acid (10 mol %) in THF at 100 °C within 3 h. <sup>b</sup> Isolated yield.

Not only enol ether **11** can be used as a  $2\pi$ -system for the indole synthesis; aldehyde **2** can also be used. For instance, the reaction of **12** with **2a** proceeded smoothly in the presence of

a catalytic amount of  $\text{Cu}(\text{OTf})_2$  in THF to give **13a** in 53% yield (eq 9). The Cu-catalyzed reaction between **12** and acetal **5a** also gave benzannulation product **13b** in 79% yield (eq 10). As we mentioned earlier, the selective formation of decarbonylated naphthalene **4b** over **3b** was attained by using the  $\text{Cu}(\text{NTf}_2)_2\text{-H}_2\text{O}$  system. However, attempts to prepare decarbonylated indole did not give any satisfactory results. For example, when the reaction of **12** with **11a** was examined using the  $\text{Cu}(\text{NTf}_2)_2\text{-H}_2\text{O}$  system, **13a** was produced in 49% yield and the desired decarbonylated indole product was obtained in less than 20% yield.



We also examined the benzofuran synthesis using furan derivatives **14**. As we expected, the reaction of **14** with propionaldehyde **2b** proceeded in the presence of  $\text{AuBr}_3$  or  $\text{Cu}(\text{OTf})_2$  catalyst to give the corresponding product **15a** in 58 and 67% yields, respectively (eq 11). The  $\text{AuBr}_3$ -catalyzed reaction of **14** with  $\beta$ -methoxystyrene **11a** also gave **15b** in 50% yield (eq 12).



## Conclusion

We are now in a position to synthesize functionalized aromatic compounds from enynals and carbonyl compounds in good to high yields. The reaction most probably proceeds through the reverse electron demand-type Diels–Alder reaction between the pyrylium intermediate and enol  $2\pi$ -system, derived from carbonyl compounds. The scope of the reaction was extended to the synthesis of benzofused heteroaromatic compounds. Further studies to elucidate the precise mechanism of

(14) Enol ethers, including furan derivatives, are known to behave as  $2\pi$ -systems. For example, see: (a) Chen, C.-H.; Rao, P. D.; Liao, C.-C. *J. Am. Chem. Soc.* **1998**, *120*, 13254. (b) Avalos, M.; Babiano, R.; Cabello, N.; Cintas, P.; Hursthouse, M. B.; Jiménez, J. L.; Light, M. E.; Palacios, J. C. *J. Org. Chem.* **2003**, *68*, 7193.

(15) For reviews, see, for instance: (a) Gilchrist, T. L. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2848. (b) Gribble, G. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1045. (c) Bräse, S.; Gil, C.; Knepper, K. *Bioorg. Med. Chem.* **2002**, *10*, 2415. (d) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873.

(16) For recent examples, see: (a) Katritzky, A. R.; Ledoux, S.; Nair, S. K. *J. Org. Chem.* **2003**, *68*, 5728 and references therein. (b) Tsuchimoto, T.; Matsubayashi, H.; Kaneko, M.; Shirakawa, E.; Kawakami, Y. *Angew. Chem., Int. Ed.* **2005**, *44*, 1336. (c) Zhang, Y.; Candelaria, D.; Herndon, J. W. *Tetrahedron Lett.* **2005**, *46*, 2211.

(17) Barluenga, J.; Vázquez-Villa, H.; Ballesteros, A.; González, J. M. *Adv. Synth. Catal.* **2005**, *347*, 526.



this reaction and to extend the scope of synthetic utility are in progress in our laboratory.

### Experimental Section

**Benzannulation between *o*-(Alkynyl)benzaldehydes (1) and Carbonyl Compounds (2).** The preparation of **3c** is representative. To a suspension of AuBr<sub>3</sub> (22 mg, 10 mol %) in 1,4-dioxane (2 mL) were added **1a** (103 mg, 0.5 mmol) and **2c** (0.084 mL, 0.6 mmol) at room temperature under Ar atmosphere. The resulting homogeneous solution was stirred at 100 °C for 3 h and then cooled to room temperature. The reaction mixture was passed through a silica gel pad using ether, and the resulting crude product was purified by column chromatography (silica gel, hexane/AcOEt = 25/1 as eluent); **3c** was obtained as a pale yellow liquid (122 mg, 0.41 mmol) in 81% yield.

**Benzannulation between 3-Phenylethynyl-1-(toluene-4-sulfonyl)-1*H*-pyrrole-2-carbaldehyde (12) and Enol Ethers (11).** The preparation of **13a** is representative. To a solution of Cu(OTf)<sub>2</sub> (9 mg, 10 mol %) and **12** (87 mg, 0.25 mmol) in THF (2 mL) was added **11a** (0.05 mL, 0.38 mmol) at room temperature under Ar atmosphere. The resulting homogeneous solution was stirred at 100

°C for 1 h and then cooled to room temperature. The reaction mixture was passed through a silica gel pad using AcOEt, and the resulting crude product was purified by column chromatography (silica gel, hexane/AcOEt = 8/1 as eluent); **13a** was obtained as a white solid (101 mg, 0.23 mmol) in 90% yield.

**Benzannulation between 3-Phenylethynyl-furan-2-carbaldehyde (14) and Carbonyl Compounds (2).** The preparation of **15a** is representative. To a solution of Cu(OTf)<sub>2</sub> (9 mg, 10 mol %) and **14** (49 mg, 0.25 mmol) in THF (2 mL) was added **2b** (0.09 mL, 1.25 mmol) at room temperature under Ar atmosphere. The resulting homogeneous solution was stirred at 100 °C for 3 h and then cooled to room temperature. The reaction mixture was passed through a silica gel pad using AcOEt, and the resulting crude product was purified by column chromatography (silica gel, hexane/AcOEt = 20/1 as eluent); **15a** was obtained as a yellow oil (40 mg, 0.17 mmol) in 67% yield.

**Supporting Information Available:** Spectroscopic and analytical data for **3a–n**, **13a–d**, and **15a–b** (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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