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AuCl-Catalyzed [4+2] Benzannulation between *o*-Alkynyl(oxo)benzene and Benzyne

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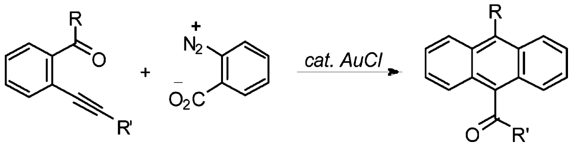
ABSTRACT



The AuCl-catalyzed benzannulation of *o*-alkynyl(oxo)benzenes with benzenediazonium 2-carboxylate proceeds under mild conditions and a variety of anthracene derivatives, having a ketone group at the 9-position, are produced in good to high yields. The reaction proceeds most probably through the [4+2] cycloaddition between benzyne and benzopyrylium auric ate complex, which would be generated by the gold-induced electrophilic cyclization of *o*-alkynyl(oxo)benzenes.

Benzynes are important reactive intermediates and many studies on their reactions have been undertaken in synthetic organic chemistry.[1] Particularly, pericyclic cycloadditions with benzyne, such as Diels−Alder reaction, are one of the most important methods for the construction of polyaromatic compounds.[2] Due to its extraordinary reactive ability, the reaction is observed with a very wide range of dienes including simple benzene derivatives or other aromatic compounds. The transition metal-catalyzed synthetic methods of polyaromatics with benzynes have been also studied well. However, to the best of our knowledge, there is no research on the Lewis acid-catalyzed Diels−Alder reaction with benzyne. We report here the AuCl-catalyzed formal [4+2] benzannulation between *o*-alkynyl(oxo)benzenes and benzenediazonium 2-carboxylate, which proceeds to give anthracene derivatives in good to high yields.[3,4]

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(1) For reviews, see: (a) Hoffmann, R. W. *Dehydrobenzene and Cycloalkynes*; Academic Press: New York, 1967. (b) Biehl, E. R.; Khanapure, S. P. *Acc. Chem. Res.* **1989**, *22*, 275−281. (c) Kessar, S. V. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 4, pp 483−515. (d) Buchward, S. L.; Broene, R. D. In *Comprehensive Organometallic Chemistry II*; Able, E. W., Stone, F. G. A., Willkinson, G., Eds.; Pergamon Press: Oxford, UK, 1995; Vol. 12, pp 771−784. (e) Pellissier, H.; Santelli, M. *Tetrahedron* **2003**, *59*, 701−730. (f) Wenk, H. H.; Winkler, M.; Sander, W. *Angew. Chem., Int. Ed.* **2003**, *42*, 502−528.

(2) For recent examples, see: (a) Schuster, I. I.; Craciun, L.; Ho, D. M.; Pascal, R. A., Jr. *Tetrahedron* **2002**, *58*, 8875−8882. (b) Duong, H. M.; Bendikov, M.; Steiger, D.; Zhang, Q.; Sonmez, G.; Yamada, J.; Wudl, F. *Org. Lett.* **2003**, *5*, 4433−4436. (c) Lu, J.; Ho, D. M.; Vogelaar, N. J.; Kraml, C. M.; Pascal, R. A., Jr. *J. Am. Chem. Soc.* **2004**, *126*, 11168−11169. (d) Ikadai, J.; Yoshida, H.; Ohshita, J.; Kunai, A. *Chem. Lett.* **2005**, *34*, 56−57. (e) Hayes, M. E.; Shinokubo, H.; Danheiser, R. L. *Org. Lett.* **2005**, *7*, 3917−3920. (f) Dockendorff, C.; Sahli, S.; Olsen, M.; Milhau, L.; Lautens, M. *J. Am. Chem. Soc.* **2005**, *127*, 15028−15029.

(3) For highlights and reviews on the Au-catalyzed reactions, see: (a) Dyker, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 4237−4239. (b) Hashmi, A. S. K. *Gold Bull.* **2003**, *36*, 3−9. (c) Hashmi, A. S. K. *Gold Bull.* **2004**, *37*, 51−65. (d) Arcadi, A.; Di Giuseppe, S. *Curr. Org. Chem.* **2004**, *8*, 795−812. (e) Hoffmann-Röder, A.; Krause, N. *Org. Biomol. Chem.* **2005**, *3*, 387−391. (f) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2005**, *44*, 6990−6993. (g) Ma, S.; Yu, S.; Gu, Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 200−203.

(4) Gold-catalyzed benzannulation, see: (a) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *J. Am. Chem. Soc.* **2000**, *122*, 11553−11554. (b) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *Org. Lett.* **2001**, *3*, 3769−3771. (c) Dankwardt, J. W. *Tetrahedron Lett.* **2001**, *42*, 5809−5812. (d) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *Catal. Today* **2002**, *72*, 19−27. (e) Mamane, V.; Hannen, P.; Fürstner, A. *Chem. Eur. J.* **2004**, *10*, 4556−4575. (f) Hashmi, A. S. K.; Rudolph, M.; Weyrauch, J. P.; Wölfle, M.; Frey, W.; Bats, J. W. *Angew. Chem., Int. Ed.* **2005**, *44*, 2798−2801. (g) Dyker, G.; Hildebrandt, D. *J. Org. Chem.* **2005**, *70*, 6093−6096. (h) Shibata, T.; Fujiwara, R.; Takano, D. *Synlett* **2005**, 2062−2066. (i) Shibata, T.; Ueno, Y.; Kanda, K. *Synlett* **2006**, 411−414. (j) Zhao, J.; Hughes, C. O.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 7436−7437. (k) Lian, J.-J.; Lin, C.-C.; Chang, H.-K.; Chen, P.-C.; Liu, R.-S. *J. Am. Chem. Soc.* **2006**, *128*, 9661−9667. (l) Hildebrandt, D.; Dyker, G. *J. Org. Chem.* **2006**, *71*, 6728−6733.

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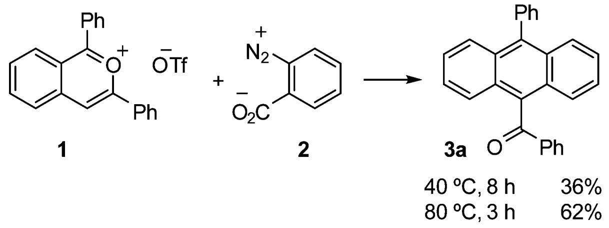
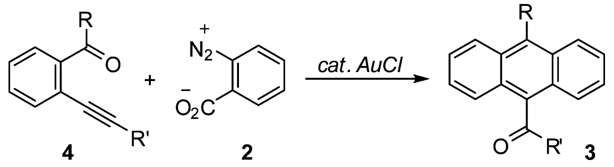
Recently, we have reported that gold-catalyzed [4+2] benzannulations between *o*-alkynyl(oxo)benzenes and alkynes proceeded smoothly in both inter- and intramolecular ways to give naphthalene compounds in good to high yields.[5] It is believed that the reaction likely proceeds through the formation of a benzopyrylium type intermediate, followed by the Diels−Alder addition of alkynes. It occurred to us that benzyne may be utilized as a partner in the benzannulation reactions. As a preliminary experiment, we initially examined the reaction of benzyne with an isolable benzo[*c*]pyrylium salt.[6,7] The requisite substrate **1** was easily prepared from the corresponding *o*-alkynyl(oxo)benzene according to the Swager's procedure,[8] and the benzannulation reaction of **1** was undertaken with benzenediazonium 2-carboxylate **2** as a precursor of benzyne. As expected, when **1** was treated with 1.8 equiv of **2** in $(ClCH_2)_2$ at 40 °C for 8 h, the reaction proceeded and an anthracene product **3a**, bearing a ketone group at the C9-position, was obtained in 36% yield (Scheme 1). It seems that the low yield of **3a** is due to the insolubility of **1** to the solvent. Indeed, the chemical yield was increased up to 62% by just conducting the reaction at 80 °C. These results clearly showed that benzyne worked as a dienophile in the Diels−Alder reaction with benzo[*c*]pyrylium salt **1** and this is a novel synthetic approach to anthracene compounds.

Scheme 1



Since the model study proceeded smoothly, we next examined the Lewis acid-catalyzed benzannulation between *o*-alkynyl(oxo)benzenes **4** and benzyne and the results are summarized in Table 1. When the reaction of (2-phenylethynyl-phenyl)-*p*-tolylmethanone **4a** (R = *p*-MeC_6H_4, R′ = Ph) was carried out with 1.8 equiv of **2** in the presence of 10 mol % of $AuBr_3$ in $(CH_2Cl)_2$, the reaction proceeded smoothly at 60 °C for 2 h and the anthracene derivative **3b** was obtained in 55% yield as a sole product (entry 1). Optimization experiments revealed that the chemical yield was increased up to 81% yield when the reaction was conducted in the presence of AuCl catalyst under 40 °C (entries 2−5). Other Lewis and Brønsted acids, such as $Cu(OTf)_2$, $PtCl_2$, and TfOH, were not effective. The AuCl-catalyzed reaction also proceeded well with other differently substituted substrates **4b**−**f** (entries 6−10). Interestingly, the reaction of **4b** with **2** produced **3a** in 72% yield (entry 6), which is higher than that of the model reaction mentioned in Scheme 1. Compared with **4a**, the reactions of **4b** and **4c** gave the corresponding products in lower yields, respectively (entries 5−7). These results would be ascribed to the fact that an intermediate **6**, having an electron-donating group as the R group, would be stabilized effectively (vide infra). The reaction of **4d**, having a propyl group instead of an aryl group at the terminus of alkyne, afforded anthracene derivative **3d** in 87% yield (entry 8). The reaction proceeded well even with the sterically bulky *tert*-butyl group (entry 9). When the reaction of **4a** was performed in the absence of gold catalyst, no benzannulation products were obtained at all. This blank test clearly indicates that a Lewis acid, such as AuCl, is an essential catalyst for the present reaction.

Table 1. The Gold-Catalyzed Benzannulation between *o*-Alkynyl(oxo)benzenes **4** and Benzenediazonium 2-Carboxylate **2**[a]



entry	4	R	R′	Lewis acid	conditions	3	yield (%)[b]
1	**4a**	*p*-MeC_6H_4	Ph	$AuBr_3$	60 °C, 2 h	**3b**	55
2	**4a**	*p*-MeC_6H_4	Ph	$AuCl_3$	60 °C, 2 h	**3b**	62
3	**4a**	*p*-MeC_6H_4	Ph	AuCl	60 °C, 1 h	**3b**	74
4[c]	**4a**	*p*-MeC_6H_4	Ph	AuCl−PPh_3	60 °C, 2 h	**3b**	52
5	**4a**	*p*-MeC_6H_4	Ph	AuCl	40 °C, 7 h	**3b**	81
6	**4b**	Ph	Ph	AuCl	40 °C, 8 h	**3a**	72
7	**4c**	*p*-$CF_3C_6H_4$	Ph	AuCl	40 °C, 9 h	**3c**	62
8	**4d**	*p*-MeC_6H_4	C_3H_7	AuCl	40 °C, 4 h	**3d**	87
9	**4e**	Ph	^{t}Bu	AuCl	40 °C, 9 h	**3e**	73
10	**4f**	2-benzofuranyl	C_3H_7	AuCl	40 °C, 9 h	**3f**	65

[a] All reaction were carried out with **4** (1 equiv) and **2** (1.8 equiv) in the presence of gold catalyst (10 mol %) in $(ClCH_2)_2$. [b] Isolated yield. [c] Starting material **4a** was recovered in 25% yield.

The preparation of **3b** is representative. To a mixture of AuCl (12 mg, 10 mol %) and **4a** (0.148 g, 0.5 mmol) in $(ClCH_2)_2$ (3.5 mL) was added a creamy white solid of benzenediazonium 2-carboxylate **2** (0.133 g, 0.9 mmol) at room temperature under Ar atmosphere. After the reaction mixture was stirred for 7 h at 40 °C, the resulting solution was filtered through a short pad of silica gel. The filtrate was evaporated under reduced pressure to give the crude product, which was purified by silica gel column chromatography with hexane/ether as eluent to give **3b** (0.151 g, 0.405 mmol) in 81% yield as a white solid.

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(5) (a) Asao, N.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12650−12651. (b) Asao, N.; Nogami, T.; Lee, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 10921−10925. (c) Asao, N.; Sato, K.; Menggenbateer; Yamamoto, Y. *J. Org. Chem.* **2005**, *70*, 3682−3685. (d) Sato, K.; Asao, N.; Yamamoto, Y. *J. Org. Chem.* **2005**, *70*, 8977−8981. (e) Asao, N. *Synlett* **2006**, 1645−1656.

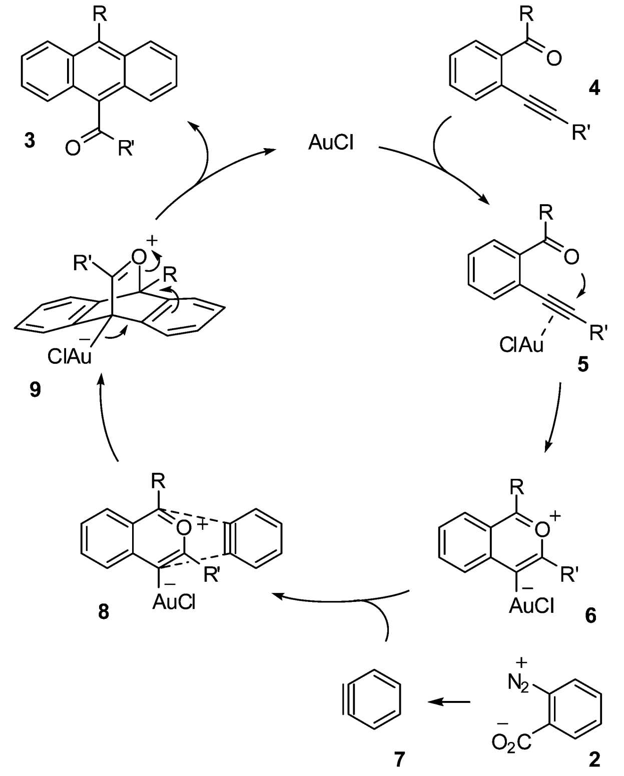
(6) Benzo[*c*]pyrylium salts are known to play a dien part in the Diels−Alder reaction with ethyl vinyl ether, see: Kuznetsov, E.; Shcherbakova, I. V.; Balaban, A. T. *Adv. Heterocycl. Chem.* **1990**, *50*, 157−254.

(7) For a review, see: Nogradi, M. In *Science of Synthesis*: *Houben-Weyl Methods of Molecular Transformations*; Georg Thieme Verlag: Stuttgart, Germany, 2003; Vol. 14, pp 201−273.

(8) Tovar, J. D.; Swager, T. M. *J. Org. Chem.* **1999**, *64*, 6499−6504.

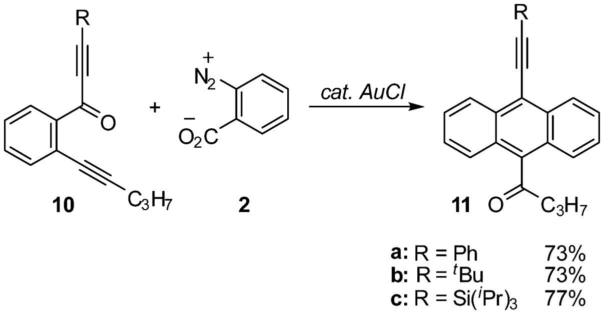
A plausible mechanism for the present benzannulation is shown in Scheme 2. The coordination of the triple bond of **4** to AuCl enhances the electrophilicity of alkyne, and the subsequent nucleophilic attack (as shown in **5**) of the carbonyl oxygen to the electron-deficient alkyne would form the ate complex **6**. The reverse electron demand-type Diels−Alder reaction between **6** and benzyne **7**, derived from **2**, would generate the intermediate **9** through **8**. The subsequent bond rearrangement, as shown in **9** with arrows, would afford the anthracene derivative **3** and regenerate AuCl.[9] Due to the instability of benzyne **7**, it is necessary that **7** should be trapped by the intermediate **6** as soon as it is generated from the precursor **2**. Probably, the generation speed of **6** is faster than that of benzyne **7** under the optimized reaction condition, which could keep the catalytic cycle effective.

Scheme 2



Introduction of alkynyl groups at the C-10 position of anthracene products was also examined. Treating **10a**−**c**, bearing an alkynyl group at the carbonyl group, with **2** in the presence of AuCl catalyst under the standard condition yielded the corresponding anthracene products **11a**−**c** in good yields, respectively (Scheme 3).

Scheme 3



We are now in a position to synthesize functionalized anthracene derivatives by the gold-catalyzed benzannulation between *o*-alkynyl(oxo)benzene **4** and benzenediazonium 2-carboxylate **2** in good to high yields. The reaction most probably proceeds through the reverse electron demand type Diels−Alder reaction between the intermediate **6** and benzyne **7**. Further studies to elucidate the precise mechanism of this reaction and to extend the scope of synthetic utility are in progress in our laboratory.

Supporting Information Available: Spectroscopic and analytical data for **3a**−**f**, **4a**−**f**, **10a**−**c**, and **11a**−**c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[9] For examples of reactions with pyrylium intermediates, see: (a) Barluenga, J.; Vázquez-Villa, H.; Ballesteros, A.; González, J. M. *J. Am. Chem. Soc.* **2003**, *125*, 9028−9029. (b) Barluenga, J.; Vázquez-Villa, H.; Ballesteros, A.; González, J. M. *Org. Lett.* **2003**, *5*, 4121−4123. (c) Zhu, J.; Germain, A. R.; Porco, J. A., Jr. *Angew. Chem., Int. Ed.* **2004**, *43*, 1239−1243. (d) Kusama, H.; Funami, H.; Takaya, J.; Iwasawa, N. *Org. Lett.* **2004**, *6*, 605−608. (e) Yue, D.; Ca, N. D.; Larock, R. C. *Org. Lett.* **2004**, *6*, 1581−1584. (f) Sato, K.; Yudha, S. S.; Asao, N.; Yamamoto, Y. *Synthesis* **2004**, 1409−1412. (g) Barluenga, J.; Vázquez-Villa, H.; Ballesteros, A.; González, J. M. *Adv. Synth. Catal.* **2005**, *347*, 526−530. (h) Kusama, H.; Funami, H.; Shido, M.; Hara, Y.; Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2005**, *127*, 2709−2716. (i) Kim, N.; Kim, Y.; Park, W.; Sung, D.; Gupta, A. K.; Oh, C. H. *Org. Lett.* **2005**, *7*, 5289−5291. (j) Gupta, A. K.; Rhim, C. Y.; Oh, C. H.; Maneb, R. S.; Han, S.-H. *Green Chem.* **2006**, *8*, 25−28. (k) Yue, D.; Cá, N. D.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 3381−3388.