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Gold-Catalyzed Domino Synthesis of Functionalized Benzofurans and Tetracyclic Isochromans via Formal Carboalkoxylation

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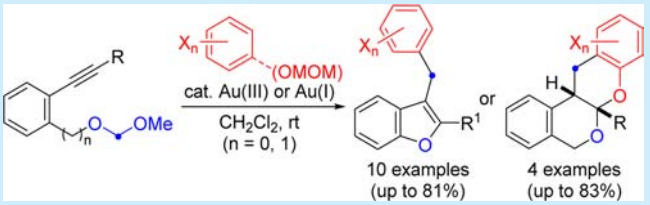
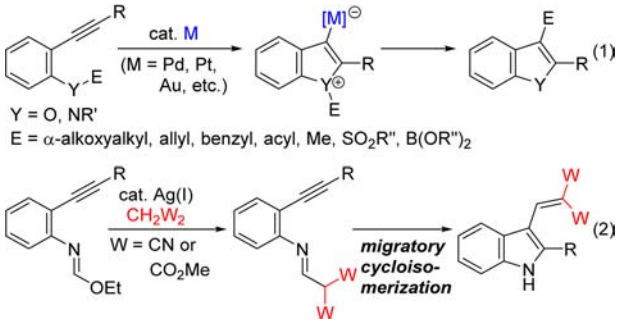
Supporting Information

ABSTRACT: A domino synthesis of benzofurans with the modification of side chains from α-alkoxyalkyl *o*-alkynylaryl ethers (n = 0) and electron-rich arenes has been developed. In the present domino reaction, which would proceed via the α-alkoxyalkylation of arenes with an intermediate in the migratory cycloisomerization of *o*-alkynylaryl ethers followed by the nucleophilic addition of benzofurans to benzyl ethers, a cationic Au(III) catalyst activates the C−C π bond and the C−O σ bond. The present method could be extended to Au(I)-catalyzed domino synthesis of tetracyclic isochromans from α-alkoxyalkyl (*o*-alkynylaryl)methyl ethers (n = 1) and aryl methoxymethyl ethers.



Transition-metal-catalyzed migratory cycloisomerization of *o*-alkynylaryl ethers and amines having a migrating group on the heteroatoms provides a powerful approach to the synthesis of 2,3-disubstituted benzofurans and indoles (eq 1),[1]



which are often found in biologically active compounds.[2] In these reactions, generally, the π-acidic metal catalyst (Pd, Pt, Au, etc.) activates the alkyne π-bond to generate an (alkenyl) metal intermediate bearing an electrophilic migrating group, which then shifts to the most nucleophilic 3-position of heterocycles. As a migrating group, α-alkoxyalkyl,[3,4] allyl,[3b,5] benzyl,[3b,6] acyl,[7] methyl,[8] sulfonyl,[9] boryl groups, and so on[10] have been employed.[11] Recently, Oh and co-workers reported an elegant synthesis of 2,3-disubstituted indoles via silver-catalyzed condensation of *N*-(*o*-alkynylaryl)formimidates and active methylene compounds followed by the migratory cycloisomerization based on the carboamination of alkynes with 1,3-alkenyl shifts (eq 2).[12] Such a domino procedure brings about not only (i) the construction of heterocyclic frameworks and (ii) the introduction of side chains but also (iii) the modification of side chains (migrating groups) in a single step and in an atom-economical manner. However, although an interesting domino reaction via the gold-catalyzed formation of *o*-alkynylphenols followed by the cycloisomerization to benzofuran has been reported by Hashmi et al.,[13] to our knowledge, the carboalkoxylation-type migratory cycloisomerization concomitant with the modification of side chains (including the formal reaction) has not been achieved. Herein, we report the unprecedented domino synthesis of benzofurans and isochromans with the modification of side chains from α-alkoxyalkyl *o*-alkynylaryl ethers and α-alkoxyalkyl (*o*-alkynylaryl)methyl ethers with arenes.

We have developed migratory cycloisomerizations of alkynes[14] and domino reactions via the formation of α,β-enone intermediates[15] for novel and efficient synthetic methods of heterocycles. As part of our research, we focused on the structure of products **2** formed by the carboalkoxylation of *o*-alkynylaryl ethers **1** with the migration of α-alkoxyalkyl groups (Scheme 1). Thus, the elimination of the alkoxy group in **2** would proceed even by weak Lewis acidity of the catalyst due to the electron donation of an oxygen atom, thereby leading to an oxonium ion intermediate **B** having an α,β-enone structure (path **a**).[16] Furthermore, in the presence of a nucleophile **3**, the intermediate **B** would be converted to benzofurans **4** with the modification of side chains by the subsequent nucleophilic addition of **3**. In the reaction of **1** and **3**, the nucleophilic addition of **3** to a zwitterionic intermediate **A** prior to the migration of the α-alkoxyalkyl group would be expected as an alternative route (path **b**). As a similar substitution reaction, a cationic gold(I)-catalyzed alkylation of alcohols, amines, and anisole with alkyl *o*-alkynylbanzoates have been reported by Asao et al.[17] One the other hand, the generated benzyl ethers **6** from **1** with electron-rich aromatics **3** (Nu = aryl) as a nucleophile would undergo the subsequent nucleophilic

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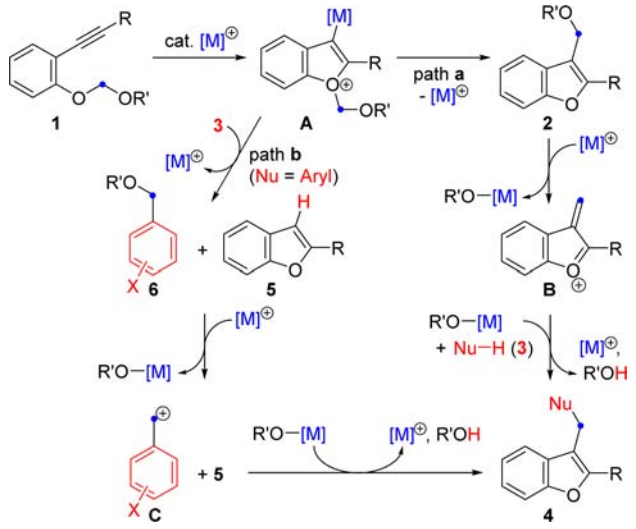
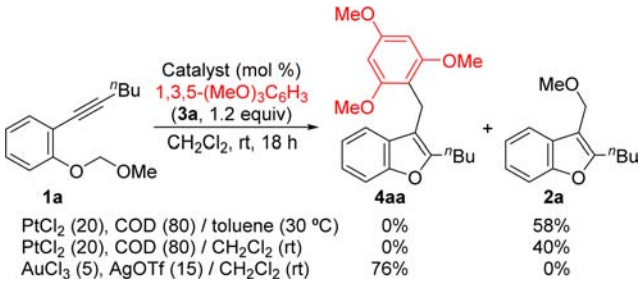
Scheme 1. Proposed Mechanism



addition of benzofurans **5** to form **4** due to the stability of the benzylic carbocation of **C** by electron-rich aromatic rings.[18] Accordingly, in both paths **a** and **b**, a good balance of π- and σ-acidity of catalytic systems would be required.

Initially, based on Yamamoto's procedure for the carboalkoxylation with the migration of α-alkoxyalkyl groups,[3a] $PtCl_2$ (20 mol %) with 1,5-cyclooctadiene (COD, 80 mol %) ligand was employed for the reaction of *o*-alkynylaryl ether **1a** with 1,3,5-trimethoxybenzene (**3a**, 1.2 equiv) in toluene or CH_2Cl_2 as a preliminary examination. Unfortunately, in these reactions, 3-(methoxymethyl)benzofuran **2a** was only obtained as a main product (Scheme 2). On the other hand, the use of the cationic

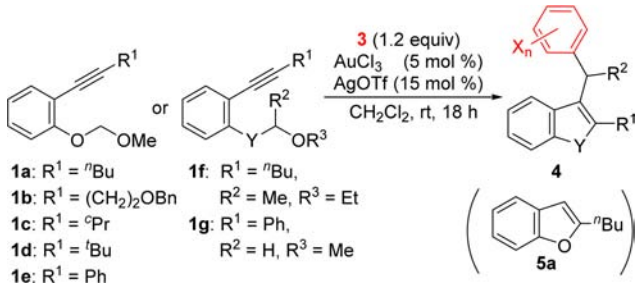
Scheme 2. Optimization of Reaction Conditions for the Domino Reaction of 1a with 3a



gold catalysts in CH_2Cl_2 led to the formation of the desired 3-benzylbenzofuran **4aa** at room temperature. In particular, gold(III) catalysts, which shows relatively high σ-electrophilicity,[19] brought about superior results to gold(I) catalysts (Supporting Information). Among tested catalysts, the catalyst derived from $AuCl_3$ (5 mol %) and AgOTf (15 mol %) afforded **4aa** in good yield (76%, Scheme 2). It should be mentioned that a sole addition of $AuCl_3$ or AgOTf resulted in the recovery of a considerable amount of **1a** (more than 86%, Supporting Information).

Under the optimized reaction conditions, the scope for the formation of **4** from *o*-alkynylaryl ethers **1** and various arenes **3** is summarized in Table 1. Similar to **1a** bearing an *n*-butyl substituent at the alkyne terminus (entry 1), benzyloxyethyl-, cyclopropyl-, and phenyl-substituted **1b**, **1c**, and **1e** reacted with 1,3,5-trimethoxybenzene (**3a**, 1.2 equiv) in the presence of

Table 1. Substrate Scope for the Formation of 4



entry	1	3[a]	4/X_n	yield[b] (%)
1	**1a**	**3a**	**4aa**/2,4,6-$(MeO)_3$	76
2	**1b**	**3a**	**4ba**/2,4,6-$(MeO)_3$	67
3	**1c**	**3a**	**4ca**/2,4,6-$(MeO)_3$	67
4	**1d**	**3a**	**4da**/2,4,6-$(MeO)_3$	26
5	**1e**	**3a**	**4ea**/2,4,6-$(MeO)_3$	81
6	**1f**	**3a**	**4fa**/2,4,6-$(MeO)_3$	28
7	**1g**	**3a**	**4ga**/2,4,6-$(MeO)_3$	57
8	**1a**	**3b**	**4ab**/2,4,5-$(MeO)_3$	52
9	**1a**	**3c**	**4ac**/2,4,5,6-$(MeO)_4$	53
10	**1a**	**3d**	**4ad**/2,4-$(MeO)_2$	00 (**5a**: 87)
11[c]	**1a**	**3e**	**4ae**/2,4,6-Me_3	17

[a] **3a**: 1,3,5-$(MeO)_3C_6H_3$, **3b**: 1,3,4-$(MeO)_3C_6H_3$, **3c**: 1,3,4,5-$(MeO)_4C_6H_2$, **3d**: 1,3-$(MeO)_2C_6H_4$, **3e**: mesitylene. [b]Isolated yields. [c]3 equiv of **3e** was used.

$AuCl_3$ (5 mol %) and AgOTf (15 mol %) at room temperature to give **4ba**, **4ca**, and **4ea** in good yields (entries 2, 3, and 5). Although the reaction of *tert*-butyl-substituted **1d** with **3a** afforded a slightly complicated mixture, the desired **4da** was obtained (entry 4). Furthermore, not only other α-alkoxyalkyl ether **1f** but also aniline **1g** could be employed as a substrate (entries 6 and 7). In addition, the present method could be applied to the reaction of **1a** with various electron-rich arenes such as 1,3,4-trimethoxybenzene (**3b**, entry 8), 1,3,4,5-tetramethoxybenzene (**3c**, entry 9), and mesitylene (**3e**, entry 11). On the other hand, the cases of 1,3-dimethoxybenzene (**3d**) gave benzofuran **5a** in 86% yield (entry 10), which was considered to be indicative of path **b** (Scheme 1) of these domino reactions.

To gain a better understanding of the involvement of path **b** in the present domino reaction, we carried out the cationic Au(III)-catalyzed reaction of benzofuran **5a** with benzyl ether **6a** or **6d** (Scheme 3a), which would be expected as an intermediate of path **b** (Scheme 1). Thus, the corresponding product **4aa** was found to be obtained in 79% yield from **5a** and **6a**, while **5a** was recovered in 94% in the reaction of **5a** and **6d**. These observations are in agreement with results in the domino reaction of **1a** with **3a** or **3d** (Table 1, entries 1 and 10). Also, considering the possibility of path **a** (Scheme 1), we examined reactions of 3-(methoxymethyl)benzofuran **2a** with arene **3a** or **3d** under the cationic Au(III)-catalyzed conditions (Scheme 3b). However, the reaction of **2a** with **3a** gave **4aa**, and that with **3d** gave **4ad**. Thus, the present domino reactions would proceed via path **b** rather than path **a** (Scheme 1). Furthermore, since the reaction of **5a** and **6a** without any catalyst did not proceed at all (Scheme 3a), the Au(III) catalyst would activate the C—O σ bond of **6a**.

Next, we attempted to extend the present method to a domino reaction of α-alkoxyalkyl (*o*-alkynylaryl)methyl ethers **7**. As a 6-membered ring formation based on the carboalkox-

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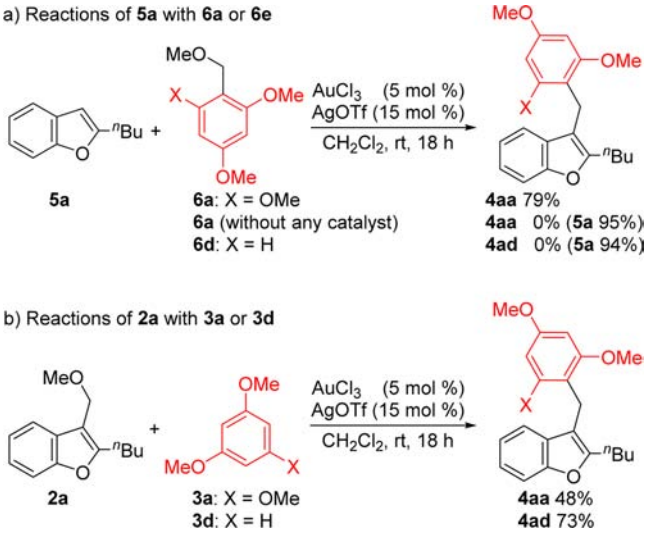
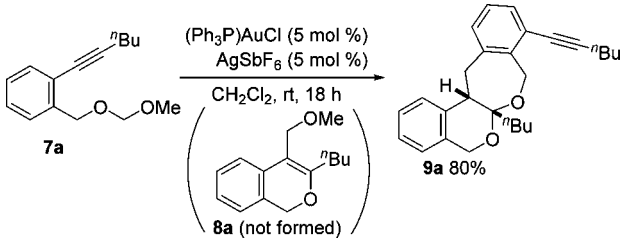
Scheme 3. Control Experiments



ylation, the migratory cycloisomerization of *o*-alkynylbenzoates bearing *α*-alkoxyalkyl[3b] and other migrating groups[11a−c] has been known, while that of (*o*-alkynylaryl)methyl ethers bearing allyl groups only has been known.[11d] Therefore, we checked whether the corresponding product **8a** was formed by the migratory cycloisomerization of **7a** (Scheme 4). Interestingly,

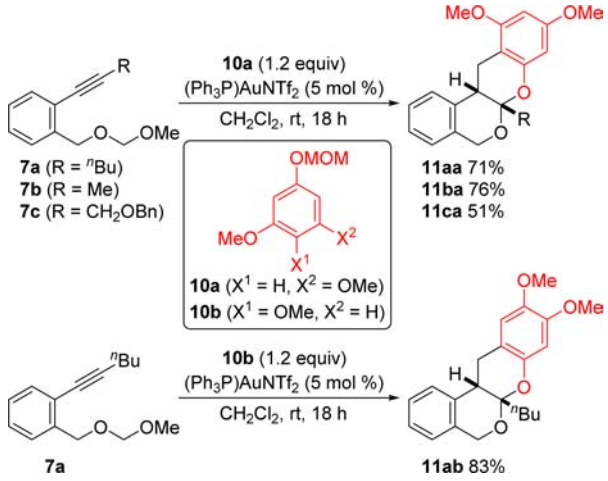
Scheme 4. Reaction of 7a without Nucleophiles



the cationic gold(I) catalyst derived from $(Ph_3P)AuCl$ (5 mol %) and $AgSbF_6$ (5 mol %) led to the formation of tetracyclic isochroman **9a**, although Yamamoto's Pt-catalytic systems ($PtCl_2$−COD in toluene)[3a] resulted in the quantitative recovery of **7a**. This result, which would be regarded as a formal annulation of **8a** with methoxymethyl-deprotected compound of **7a**, encouraged us to examine the cationic gold-catalyzed domino reaction of **7** with various arenes (Scheme 5 and the Supporting Information).

At the outset, it turned out that the reaction of (*o*-alkynylaryl)methyl ether **7a** with 1,3,5-trimethoxybenzene (**3a**, 1.2 equiv) under gold-catalyzed conditions gave a complicated mixture (Supporting Information). However, when **7a** reacted with aryl methoxymethyl ether **10a** in the presence of $(Ph_3P)AuNTf_2$ (Gagosz catalyst)[20] in CH_2Cl_2 at room temperature, tetracyclic isochroman **11aa** was obtained in 71% yield (Scheme 5). Furthermore, Gagosz catalyst could be applied to reactions of **7a**−**c** with **10a** or **10b**, thereby leading to the corresponding tetracyclic isochromans **11** in 51−83% yields. The obtained tetracyclic isochromans **9a** and **11** were single *cis*-isomers that were determined by the X-ray structure analysis of **11aa**[21] and by NOE experiments of other products. It should be mentioned that cationic Au(III) catalyst showed

Scheme 5. Reactions of 7a−d with 10a or 10b



inferior results to the Gagosz catalyst (Supporting Information).

In conclusion, we have developed the cationic gold(III)-catalyzed domino synthesis of benzofurans with the modification of side chains from *α*-alkoxyalkyl *o*-alkynylaryl ethers and electron-rich arenes. Mechanistic studies imply that the present domino reactions proceed via nucleophilic addition of benzofurans to benzyl ethers, which are formed by the *α*-alkoxyalkylation of arenes (path **b**). The present method could be extended to gold(I)-catalyzed domino synthesis of tetracyclic isochromans from *α*-alkoxyalkyl (*o*-alkynylaryl)-methyl ethers and arenes. Further investigations will focus on extending this strategy to other heterocyclic synthesis.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b02159.

Screening of catalysts for the domino reactions of **1a** and **7a**, experimental procedures, and spectral data (PDF)
Crystallographic data of **11aa** (CIF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For recent reviews, see: (a) Dudnik, A.; Chernyak, N.; Gevorgyan, V. *Aldrichimica Acta* **2010**, *43*, 37. (b) Gulevich, A. V.; Dudnik, A. S.; Chernyak, N.; Gevorgyan, V. *Chem. Rev.* **2013**, *113*, 3084. (c) Weibel, J.-M.; Blanc, A.; Pale, P. *Chem. Rev.* **2008**, *108*, 3149. (d) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873. (e) Shapiro, N. D.; Toste, F. D. *Synlett* **2010**, *2010*, 675. (f) Pflästerer, D.; Hashmi, A. S. K. *Chem. Soc. Rev.* **2016**, *45*, 1331.

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Org. Lett. 2016, 18, 4136−4139

(2) Recent examples: (a) Lu, Z.; Ott, G. R.; Anand, R.; Liu, R.-Q.; Covington, M. B.; Vaddi, K.; Qian, M.; Newton, R. C.; Christ, D. D.; Trzaskos, J.; Duan, J. J.-W. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 1958. (b) Gessner, G.; Macianskiene, R.; Starkus, J. G.; Schoenherr, R.; Heinemann, S. H. *Eur. J. Pharmacol.* **2010**, *632*, 52. (c) Suresh, N.; Vasanthi, N. S. *J. Proteomics Bioinf.* **2010**, *3*, 20. (d) Li, J.; Pan, L.; Deng, Y.; Muñoz-Acuña, U.; Yuan, C.; Lai, H.; Chai, H.; Chagwedera, T. E.; Farnsworth, N. R.; Carcache de Blanco, E. J.; Li, C.; Soejarto, D. D.; Kinghorn, A. D. *J. Org. Chem.* **2013**, *78*, 10166. (e) Saravanan, B.; Saravanan, R. R.; Manivannan, V. *J. Chem. Pharm. Res.* **2012**, *4*, 3057.

(3) (a) Nakamura, I.; Mizushima, Y.; Yamamoto, Y. *J. Am. Chem. Soc.* **2005**, *127*, 15022. (b) Fürstner, A.; Davies, P. W. *J. Am. Chem. Soc.* **2005**, *127*, 15024. (c) Fürstner, A.; Heilmann, E. K.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 4760. (d) Nakamura, I.; Chan, C. S.; Araki, T.; Terada, M.; Yamamoto, Y. *Adv. Synth. Catal.* **2009**, *351*, 1089. Examples of sulfide analogues: (e) Nakamura, I.; Sato, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 4473. (f) Nakamura, I.; Okamoto, M.; Sato, T.; Terada, M. *Heterocycles* **2010**, *82*, 689.

(4) Representative examples for the gold-catalyzed reactions of alkynes and acetals: (a) Zhang, G.; Zhang, L. *J. Am. Chem. Soc.* **2008**, *130*, 12598. (b) Bae, H. J.; Jeong, W.; Lee, J. H.; Rhee, Y. H. *Chem. - Eur. J.* **2011**, *17*, 1433. (c) Zhang, M.; Wang, Y.; Yang, Y.; Hu, X. *Adv. Synth. Catal.* **2012**, *354*, 981. (d) Zi, W.; Toste, F. D. *J. Am. Chem. Soc.* **2013**, *135*, 12600. (e) Schultz, D. M.; Babij, N. R.; Wolfe, J. P. *Adv. Synth. Catal.* **2012**, *354*, 3451. (f) Yu, Y.; Yang, W.; Rominger, F.; Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2013**, *52*, 7586.

(5) (a) Cacchi, S.; Fabrizi, G.; Moro, L. *Synlett* **1998**, *1998*, 741. (b) Monteiro, N.; Balme, G. *Synlett* **1998**, *1998*, 746. (c) Cacchi, S.; Fabrizi, G.; Moro, L. *Tetrahedron Lett.* **1998**, *39*, 5101. (d) Liang, Z.; Ma, S.; Yu, J.; Xu, R. *J. Org. Chem.* **2007**, *72*, 9219. (e) Cacchi, S.; Fabrizi, G.; Pace, P. *J. Org. Chem.* **1998**, *63*, 1001. (f) Majumdar, K. C.; Hazra, S.; Roy, B. *Tetrahedron Lett.* **2011**, *52*, 6697. (g) Propargyl groups: Cacchi, S.; Fabrizi, G.; Moro, L. *Tetrahedron Lett.* **1998**, *39*, 5101. (h) See: Fürstner, A.; Szillat, H. *J. Am. Chem. Soc.* **2001**, *123*, 11863.

(6) Examples of sulfide and selenide analogues: (a) Nakamura, I.; Sato, T.; Terada, M.; Yamamoto, Y. *Org. Lett.* **2008**, *10*, 2649. (b) Sato, T.; Nakamura, I.; Terada, M. *Eur. J. Org. Chem.* **2009**, *2009*, 5509.

(7) (a) Shimada, T.; Nakamura, I.; Yamamoto, Y. *J. Am. Chem. Soc.* **2004**, *126*, 10546. (b) Nakamura, I.; Mizushima, Y.; Yamagishi, U.; Yamamoto, Y. *Tetrahedron* **2007**, *63*, 8670. (c) Nakamura, I.; Sato, Y.; Konta, S.; Terada, M. *Tetrahedron Lett.* **2009**, *50*, 2075. (d) Wu, C. Y.; Hu, M.; Liu, Y.; Song, L. J.; Lei, Y.; Tang, B. X.; Li, R. J.; Li, J. H. *Chem. Commun.* **2012**, *48*, 3197.

(8) Zeng, X.; Kinjo, R.; Donnadieu, B.; Bertrand, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 942.

(9) (a) Nakamura, I.; Yamagishi, U.; Song, D.; Konta, S.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 2284. (b) Nakamura, I.; Yamagishi, U.; Song, D.; Konta, S.; Yamamoto, Y. *Chem. - Asian J.* **2008**, *3*, 285. (c) Zhu, Z.; Chen, K.; Xu, Q.; Shi, M. *Adv. Synth. Catal.* **2015**, *357*, 3081.

(10) (a) Hirner, J. J.; Faizi, D. J.; Blum, S. A. *J. Am. Chem. Soc.* **2014**, *136*, 4740. (b) Chong, E.; Blum, S. A. *J. Am. Chem. Soc.* **2015**, *137*, 10144. (c) Faizi, D. J.; Issaian, A.; Davis, A. J.; Blum, S. A. *J. Am. Chem. Soc.* **2016**, *138*, 2126. (d) Silyl migration of sulfide analogues: Nakamura, I.; Sato, T.; Terada, M.; Yamamoto, Y. *Org. Lett.* **2007**, *9*, 4081.

(11) Migratory cycloisomerizations of *o*-alkynylbenzoates: (a) Allyl groups: Shi, Y.; Roth, K. E.; Ramgren, S. D.; Blum, S. A. *J. Am. Chem. Soc.* **2009**, *131*, 18022. (b) Benzyl and cinnamyl groups: Hashmi, A. S. K.; Lothschütz, C.; Döpp, R.; Ackermann, M.; De Buck Becker, J.; Rudolph, M.; Scholz, C.; Rominger, F. *Adv. Synth. Catal.* **2012**, *354*, 133. (c) Benzyl group: Komeyama, K.; Takahashi, K.; Takaki, K. *Org. Lett.* **2008**, *10*, 5119. (d) A migratory cycloisomerization of (*o*-alkynylaryl)methyl ethers with the migration of allyl groups: Ackermann, M.; Bucher, J.; Rappold, M.; Graf, K.; Rominger, F.; Hashmi, A. S. K. *Chem. - Asian J.* **2013**, *8*, 1786.

(12) (a) Oh, C. H.; Karmakar, S.; Park, H. S.; Ahn, Y. C.; Kim, J. W. *J. Am. Chem. Soc.* **2010**, *132*, 1792. (b) Oh, C. H.; Park, H. S.; Park, N.; Kim, S. Y.; Piao, L. *Synlett* **2014**, *25*, 579. (c) See also: Kusama, H.; Miyashita, Y.; Takaya, J.; Iwasawa, N. *Org. Lett.* **2006**, *8*, 289. (d) Kamijo, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 11940.

(13) This reaction is a first example for gold-catalyzed cycloisomerization of *o*-alkynylphenols. See: (a) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *Org. Lett.* **2001**, *3*, 3769. The author succeeded isolating the organogold intermediates of these cycloisomerization. See also: (b) Hashmi, A. S. K.; Ramamurthi, T. D.; Rominger, F. *Adv. Synth. Catal.* **2010**, *352*, 971.

(14) (a) Saito, A.; Kanno, A.; Hanzawa, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 3931. (b) Saito, A.; Oda, S.; Fukaya, H.; Hanzawa, Y. *J. Org. Chem.* **2009**, *74*, 1517. (c) Saito, A.; Konishi, T.; Hanzawa, Y. *Org. Lett.* **2010**, *12*, 372. (d) Saito, A.; Iimura, K.; Hanzawa, Y. *Tetrahedron Lett.* **2010**, *51*, 1471. (e) Saito, A.; Enomoto, Y.; Hanzawa, Y. *Tetrahedron Lett.* **2011**, *52*, 4299.

(15) (a) Saito, A.; Umakoshi, M.; Yagyu, N.; Hanzawa, Y. *Org. Lett.* **2008**, *10*, 1783. (b) Saito, A.; Kasai, J.; Odaira, Y.; Fukaya, H.; Hanzawa, Y. *J. Org. Chem.* **2009**, *74*, 5644. (c) Saito, A.; Kasai, J.; Konishi, T.; Hanzawa, Y. *J. Org. Chem.* **2010**, *75*, 6980.

(16) (a) Box, V. G. S.; Jackson, Y. A. *Heterocycles* **1983**, *20*, 753. (b) Jackson, Y. A.; Marriott, K.-S. C.; Anderson, M. *Heterocycles* **2001**, *55*, 91. (c) Maguire, A. R.; Plunkett, S. J.; Papot, S.; Clynes, M.; O'Connor, R.; Touhey, S. *Bioorg. Med. Chem.* **2001**, *9*, 745. (d) Campbell, J. A.; Bordunov, V.; Broka, C. A.; Dankwardt, J.; Hendricks, R. T.; Kress, J. M.; Walker, K. A. M.; Wang, J.-H. *Tetrahedron Lett.* **2004**, *45*, 3793.

(17) (a) Asao, N.; Aikawa, H.; Tago, S.; Umetsu, K. *Org. Lett.* **2007**, *9*, 4299. (b) Aikawa, H.; Tago, S.; Umetsu, K.; Haginiwa, N.; Asao, N. *Tetrahedron* **2009**, *65*, 1774. See also: (c) Li, Y.; Yang, Y.; Yu, B. *Tetrahedron Lett.* **2008**, *49*, 3604. (d) Tang, Y.; Li, J.; Zhu, Y.; Li, Y.; Yu, B. *J. Am. Chem. Soc.* **2013**, *135*, 18396.

(18) In the transition-metal-catalyzed benzylation of indoles with benzyl alcohol, the stability of the benzylic carbocation is critical to the success of these reactions. (a) Au(III) catalyst: Hikawa, H.; Suzuki, H.; Azumaya, I. *J. Org. Chem.* **2013**, *78*, 12128. (b) Ru(II) catalyst: Putra, A. E.; Takigawa, K.; Tanaka, H.; Ito, Y.; Oe, Y.; Ohta, T. *Eur. J. Org. Chem.* **2013**, *2013*, 6344. (c) Ir(I) catalyst: Whitney, S.; Grigg, R.; Derrick, A.; Keep, A. *Org. Lett.* **2007**, *9*, 3299.

(19) (a) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395. (b) Yamamoto, Y. *J. Org. Chem.* **2007**, *72*, 7817. (c) See also ref 18a.

(20) Mézailles, N.; Ricard, L.; Gagosz, F. *Org. Lett.* **2005**, *7*, 4133.

(21) CCDC 1481371 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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