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Novel Carbon−Carbon Bond Formation from Propargylic Alcohols and Olefin toward Five-Membered Heterocyclic Rings Catalyzed by $AgSbF_6$

Ke-Gong Ji, Xing-Zhong Shu, Shu-Chun Zhao, Hai-Tao Zhu, Yan-Ning Niu, Xue-Yuan Liu, and Yong-Min Liang*

State Key Laboratory of Applied Organic Chemistry, Lanzhou University, and State Key Laboratory of Solid Lubrication, Lanzhou Institute of Chemical Physics, Chinese, Academy of Science, Lanzhou 730000, P. R. China

liangym@lzu.edu.cn

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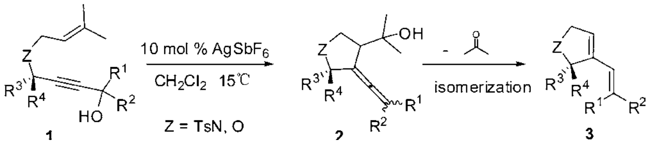
ABSTRACT

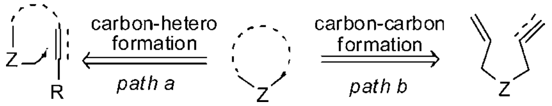


A mild and direct process for C−C bond formation from propargylic alcohols and olefin has been developed in the presence of a silver catalyst. In this reaction, trace amounts of water were necessary and allene alcohols 2 and 1,3-dienes 3 were obtained selectively.

The development of novel methods for the annulation of five-membered heterocyclic rings is very important in the field of synthetic organic chemistry because such heterocyclic compounds are useful synthetic intermediates as well as important structural units found in natural and artificial products.[1] For example, kainic acid and allokainic acid, isolated from marine alga, attract the interest of synthetic chemists.[2]

Recently, transition-metal-catalyzed cyclization reactions of carbon-hetero formation (via *path a*) and carbon−carbon formation (via *path b*) represent an effective and straightforward methodology for the synthesis of this heterocyclic compounds (Scheme 1).[3]

Scheme 1



Silver "catalysts", as a transition metal catalyst, are commonly considered to have low efficiency and not to be as good as other late transition metals. On the other hand, silver(I) complexes are generally used as stoichiometric oxidants for the oxidation of various organic or inorganic substrates. Many reports used silver(I) complexes as catalysts

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(1) (a) Porter, A. E. A. *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, 1984; Vol. 3, pp 157−197. (b) Sainsburg, M. *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, 1984; Vol. 3, pp 995−1038. (c) Sharp, J. T. *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, 1984; Vol. 7, pp 593−651.

(2) Takano, S.; Sugihara, T.; Satoh, S.; Ogasawara, K. *J. Am. Chem. Soc.* **1988**, *110*, 6467, and references therein.

(3) For recent reviews, see: (a) Patil, N. T.; Yamamoto, Y. *Chem. Rev.* **2008**, *108*, 3395. (b) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (c) McReynolds, M. D.; Dougherty, J. M.; Hanson, P. R. *Chem. Rev.* **2004**, *104*, 2239. (d) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079. (e) Deiters, A.; Martin, S. F. *Chem. Rev.* **2004**, *104*, 2199. (f) Zeni, G.; Larock, R. C. *Chem. Rev.* **2004**, *104*, 2285. (g) Yet, L. *Chem. Rev.* **2000**, *100*, 2963. (h) Tsuji, J. *Transition Metal Reagents and Catalysts*; John Wiley & Sons Ltd.: New York, 2000. (i) *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH Verlag GmbH: Weinheim, 1998. (j) *Transition Metal Catalyzed Reactions*; Murahashi, S., Davies, S. G., Eds.; Blackwell Science: Oxford, 1999.

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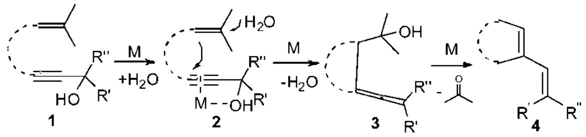
in oxidation or group-transfer reactions,[4] although recent studies have shown that silver species exhibited interesting catalytic activities functioning for carbon-hetero formation.[5,6] However, examples of the carbocyclization catalyzed by silver are limited.[7] In the context of our ongoing efforts to develop tandem reactions, we anticipated that a new domino process initiated by silver induced C−C bond formation followed by subsequent trace amounts of water attack (Scheme 2) might be achieved. Herein, we reported a novel carbon−carbon bond formation from propargylic alcohols and olefin toward five-membered heterocyclic rings in the presence of $AgSbF_6$. In this reaction, trace amounts of water were necessary and olefin as the intramolecular nucleophilic with propargylic alcohols were selectively transformed into allene alcohols and 1,3-dienes.

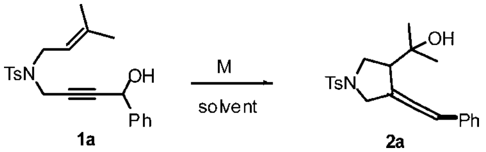
Scheme 2



Initially, we started by using 0.3 mmol of N-(4-hydroxy-4-phenylbut-2-ynyl)-N-(3-methylbut-2-enyl)-toluenesulfonamide **1a** and 5 mol % of $AgSbF_6$ in wet CH_2Cl_2 at room temperature; to our delight, the desired product 2-(4-(2-phenylvinylidene)-1-tosylpyrrolidin-3-yl)propan-2-ol **2a** was formed in 80% yield after 20 h. On increasing the amount of catalyst to 10 mol %, a 88% yield of **2a** was obtained after 15 h, when the silver salt was added to 15 mol %, but no higher yield was obtained (Table 1, entries 1−3). Then we decrease temperature to 15 °C, an excellent yield of **2a** was obtained with 10 mol % $AgSbF_6$ (up to 92%) (Table 1, entry 4). The reaction was also tested in dry CH_2Cl_2 at 15 °C; only trace amounts of **2a** was observed (Table 1, entry 6). Other silver catalysts, such as AgOTf, $AgBF_4$, $AgNTf_2$, $AgOOCCF_3$ gave no better results (Table 1, entries 7−10). $AlCl_3$ and $FeCl_3$, including protic acids such as TsOH, TFA and TfOH have also been applied to the reaction, no superior results were obtained (Table 1, entries 11−15). Other solvents were also tested in the reaction, only DCE gave good yield. Thus, the use of $AgSbF_6$ (10 mol %) in wet CH_2Cl_2 at 15 °C was found to be the most efficient and used as the standard conditions.

With the optimized conditions in hand, various representative propargylic alcohols **1a−l** were then submitted to the

Table 1. Transition-Metal Catalysts for the Transformation of **1a** to **2a**

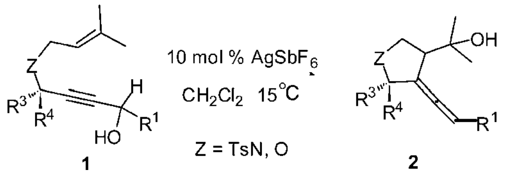


1a **2a**

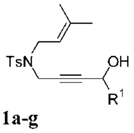
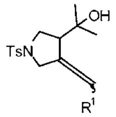
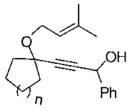
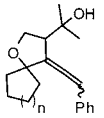
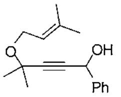
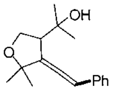
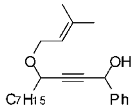
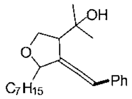
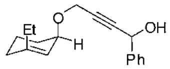
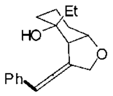
entry	catalyst (mol %)	solvent	temp (°C)	time (h)	yield (%)[a]
1	$AgSbF_6$ (5)	CH_2Cl_2	rt	20	80
2	$AgSbF_6$ (10)	CH_2Cl_2	rt	15	88
3	$AgSbF_6$ (15)	CH_2Cl_2	rt	12	87
4	$AgSbF_6$ (10)	CH_2Cl_2	15	20	92
5	$AgSbF_6$ (10)	CH_2Cl_2	0	24	80
6	$AgSbF_6$ (10)	dry CH_2Cl_2	15	24	[c]
7	AgOTf (10)	CH_2Cl_2	15	24	0
8	$AgBF_4$(10)	CH_2Cl_2	15	24	0
9	$AgNTf_2$ (10)	CH_2Cl_2	15	24	73
10[b]	$AgOOCCF_3$ (10)	CH_2Cl_2	15	24	0
11	$AlCl_3$ (10)	CH_2Cl_2	15	24	0
12	$FeCl_3$ (10)	CH_2Cl_2	15	24	[c]
13	TsOH (10)	CH_2Cl_2	15	24	13
14	F_3CCOOH (10)	CH_2Cl_2	15	24	[c]
15[b]	TfOH(10)	CH_2Cl_2	15	24	[d]
16	$AgSbF_6$ (10)	$ClCH_2CH_2Cl$	15	18	91
17	$AgSbF_6$ (10)	THF	15	24	0
18	$AgSbF_6$ (10)	CH_3OH	15	24	0
19	$AgSbF_6$ (10)	toluene	15	24	0
20	$AgSbF_6$ (10)	CH_3NO_2	15	24	0

[a] Isolated yield. [b] Decomposed. [c] Trace. [d] For details, see Supporting Information.

Table 2. $AgSbF_6$−Catalyzed Synthesis of Allene Alcohols **2** from Propargylic Alcohols **1**[a]

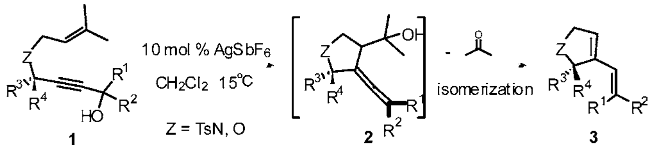


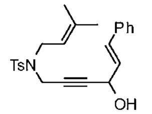
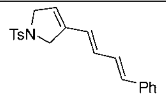
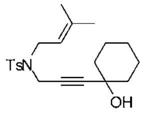
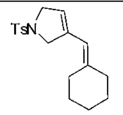
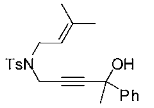
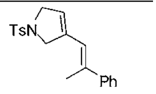
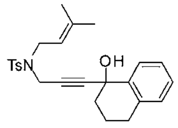
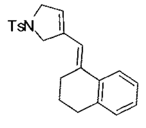
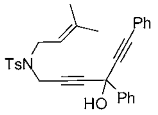
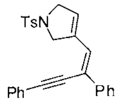
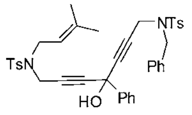
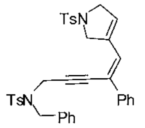
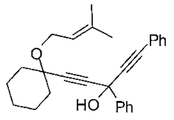
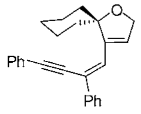
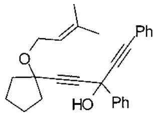
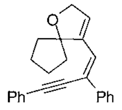
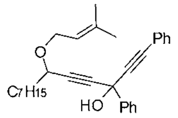
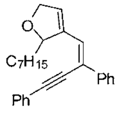
1 **2**

entry	substrate	product		time (h)	yield (%)[b]
1	 **1a-g**	 **2a-g**	**2a**, $R^1 = Ph$	20	92
2			**2b**, $R^1 = p\text{-}ClC_6H_4$	15	94
3			**2c**, $R^1 = p\text{-}CH_3C_6H_4$	4.5	67
4			**2d**, R^1 = furan	12	73
5			**2e**, $R^1 = m\text{-}CH_3C_6H_4$	14	73
6			**2f**, $R^1 = o\text{-}FC_6H_4$	12	68
7			**2g**, $R^1 = C_2H_5$	24	0
8	 **1h-i**	 **2h-i**	**2h**, n = 1	20	60
9			**2i**, n = 0	12	65
10	 **1j**	 **2j**		16	54
11	 **1k**	 **2k**		17	67
12	 **1l**	 **2l**		24	0

[a] Conditions: 0.3 mmol of **1** with 10 mol % of catalyst in CH_2Cl_2 (2.0 mL) at 15 °C. [b] Isolated yield.

Table 3. $AgSbF_6$-Catalyzed Synthesis of 1,3-dienes **3** from Propargylic Alcohols **1**[a]



substrate **1**	product **2**[b]	substrate **1**	product **2**[b]	substrate **1**	product **2**[b]
 **1m** time:10 h	 **3m** yield = 50%	 **1n** time:11 h	 **3n** yield = 95% [c]	 **1o** time:12 h	 **3o** yield = 87%
 **1p** time:3 h	 **3p** yield = 81%	 **1q** time:2 h	 **3q**[7] yield = 81%	 **1r** time:3 h	 **3r** yield = 90%
 **1s** time:5 h	 **3s** yield = 97%	 **1t** time:7 h	 **3t** yield = 80%	 **1u** time:17 h	 **3u** yield = 86%

[a] Conditions: 0.3 mmol of **1** with 10 mol % of catalyst in CH_2Cl_2 (2.0 mL) at 15 °C. [b] Isolated yield. [c] The reaction was carried out at 40 °C.

above conditions, as depicted in Table 2. Thus, a tandem carbon−carbon and carbon−oxygen bond formation of propargylic alcohols **1a**−**f** and **1h**-**k** proceeded smoothly to provide corresponding products **2a**−**f** and **2h**−**k** in moderate to excellent yields. The reaction works well with aromatic R^1 groups. Electron-withdrawing aryl groups showed better results than those with an electron-rich group in this tandem reaction (**1b** vs **1c**). Substrate **1d** with a heteroaromatic R^1 group can also afford the desired product **2d** in 73% yield, while a substrate like **1g** with an aliphatic R^1 group gave no reaction. Other substrates like **1h**−**k** can also afford corresponding furan derivatives **2h**−**k** in moderate yield. Interestingly, substrate like **1l** with steric effects gave no reaction.

Furthermore, to expand the scope of this reaction, we also investigated a range of propargylic alcohols; it was found that under the silver catalyst some substrates **1** transferred into 1,3-dienes **3** directly, without giving the products **2** as depicted in Table 3. Various representative propargylic alcohols **1m**−**u** transferred into corresponding products **3m**−**u** in moderate to excellent yields (up to 97%) (Figure 1).

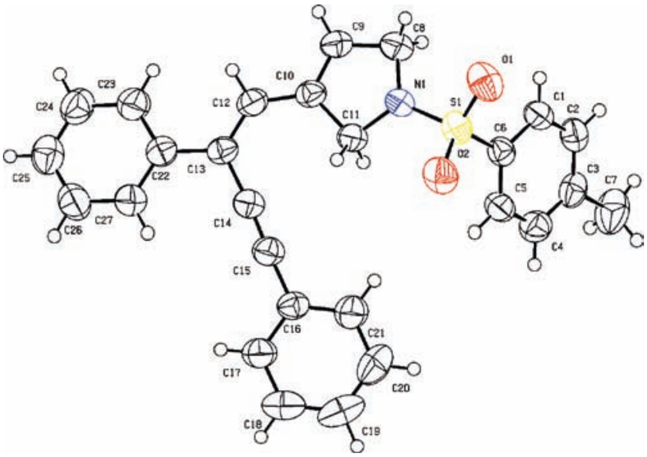


Figure 1. X-ray structure of **3q**.[8]

To uncover the mechanism for the reaction, we started out by using propargylic alcohol **1m** under the standard conditions, and the desired product **2m** was isolated in 30%

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(4) For selected papers, see: (a) Li, Z.; Capretto, D. A.; Rahaman, R.; He, C. *Angew. Chem., Int. Ed.* **2007**, *46*, 5184. (b) Cui, Y.; He, C. *Angew. Chem., Int. Ed.* **2004**, *43*, 4210. (c) Clark, T. B.; Woerpel, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 9522. (d) Cui, Y.; He, C. *J. Am. Chem. Soc.* **2003**, *125*, 16202. (e) Josephsohn, N. S.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 4018. (f) Momiyama, N.; Yamamoto, H. *J. Am. Chem. Soc.* **2003**, *125*, 6038. (g) Dias, H. V. R.; Browning, R. G.; Polach, S. A.; Diyabalanage, H. V. K.; Lovely, C. J. *J. Am. Chem. Soc.* **2003**, *125*, 9270.

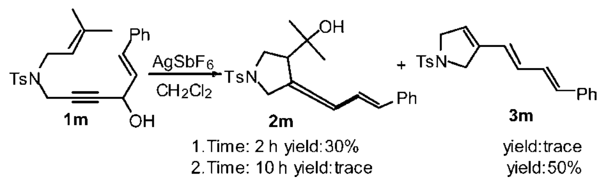
(5) For selected recent examples of Ag-catalyzed reviews, see: (a) Yamamoto, Y. *Chem. Rev.* **2008**, *108*, 3199. (b) Weibel, J.-M.; Blanc, A.; Pale, P. *Chem. Rev.* **2008**, *108*, 3149. (c) Álvarez-Corral, M.; Muñoz-Dorado, M.; Rodríguez-García, I. *Chem. Rev.* **2008**, *108*, 3174. (d) Li, Z.; He, C. *Eur. J. Org. Chem.* **2006**, 4313.

(6) For selected examples of Ag-catalyzed reactions, see: (a) Umeda, R.; Studer, A. *Org. Lett.* **2008**, *10*, 993. (b) Mandai, H.; Mandai, K.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 17961. (c) Yong, S. W.; Eom, J. I. *J. Org. Chem.* **2006**, *71*, 6705. (d) Yang, C.-G.; Reich, N. W.; Shi, Z.; He, C. *Org. Lett.* **2005**, *7*, 4553. (e) Yao, X.; Li, C.-J. *Org. Lett.* **2005**, *7*, 4395. (f) Patil, N. T.; Pahadi, N. K.; Yamamoto, Y. *J. Org. Chem.* **2005**, *70*, 10096. (g) Wei, C.; Li, Z.; Li, C.-J. *Org. Lett.* **2003**, *5*, 4473.

(7) (a) Yao, X.; Li, C.-J. *J. Org. Chem.* **2005**, *70*, 5752. (b) Harrison, T. J.; Dake, G. R. *Org. Lett.* **2004**, *6*, 5023. (c) Sweis, R. F.; Schramm, M. P.; Kozmin, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 7442.

yield after 2 h,[9] and only a trace amount of **3m** was observed. When the reaction was carried out for 10 h under the above conditions, and only a trace amount of **2m** was observed; also, a 50% yield of **3m** was isolated (Scheme 3).

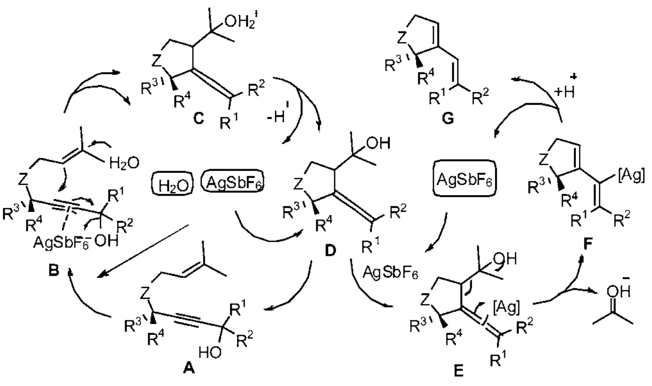
Scheme 3



On the basis of the above observations, we propose the following plausible mechanisms for this cascade transformation (Scheme 4). (i) Coordination of the alkynyl moiety and hydroxy of **A** to $AgSbF_6$ gives the complex **B**. (ii) The subsequent domino trace amounts of water as the nucleophilic attack the olefin and occurs carbocyclization affords intermediate allene alcohol cation **C**. (iii) Intermediate **C** releases the hydrogen cation to afford the allene alcohol **D** and regenerates the catalyst $AgSbF_6$. (iv) Coordination of the allene moiety of **D** to Ag catalyst gives the complex **E**. (v) Some of allene alcohols occur domino carbon−carbon bond cleavage and afford the intermediate **F**. (IV) Protonation of **F** yields 1,3-dienes **G** and regenerates the catalyst Ag. In this reaction, trace amounts of water played an important role.

In summary, a mild and direct process for C−C bond formation from propargylic alcohols and olefin has been developed in the presence of a silver catalyst. In this reaction, trace amounts of water were necessary and propargylic alcohols with olefin were selectively transformed into five-member heterocyclic compounds allene alcohols **2** and 1,3-dienes **3** containing various functionalities. A more detailed investigation on the mechanism, as well as the scope of this cascade, is ongoing in our laboratory.

Scheme 4. Proposed Mechanism



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Supporting Information Available: Experimental procedures and full spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) The molecular structure of the corresponding product **1q** was determined by means of X-ray crystallographic studies; for details, see the Supporting Information.

(9) The product **2m** may be not stable, and only 30% yield was isolated by flash column chromatography.