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# Gold-Catalyzed Double Migration-Benzannulation Cascade toward Naphthalenes

**Alexander S. Dudnik, Todd Schwier, and Vladimir Gevorgyan***

*Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, Illinois 60607-7061*

*vlad@uic.edu*

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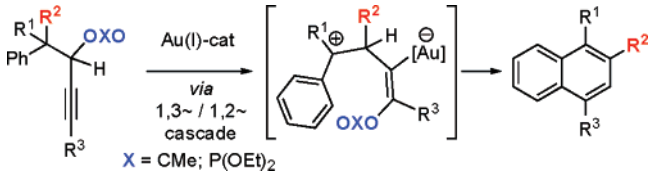
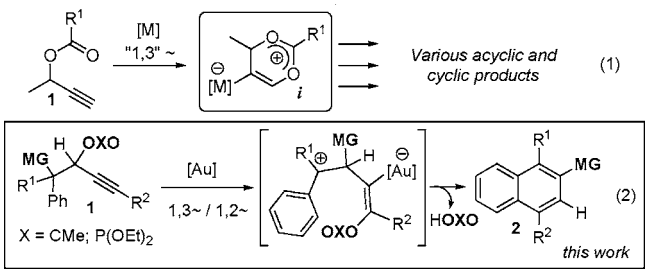
## ABSTRACT




**A novel gold(I)-catalyzed cycloisomerization of propargylic esters leading to unsymmetrically substituted naphthalenes has been developed. This cascade reaction involves an unprecedented tandem sequence of 1,3- and 1,2-migration of two different migrating groups. It is believed that this transformation likely proceeds via the formation of 1,3-diene intermediate or its precursor, which upon cyclization and aromatization steps transforms into the naphthalene core.**

In recent years, transition-metal-catalyzed transformations of propargylic esters[1] have received much attention. Particularly intriguing is reactivity of these easily accessible compounds in the context of gold catalysis,[2] which has been reflected in the development of a variety of diverse and elegant transformations leading to an immense array of complex organic molecules. Remarkable propensity of propargylic esters **1** to undergo 1,3-acyl migration,[1,2] through the formation of an activated allene equivalent, intermediate ***i***,[1] allowed for efficient and expeditious assembly of various acyclic unsaturated synthons[3] and complex carbo-[4] and heterocycles[5] (eq 1). Herein, we wish to report a gold(I)-catalyzed double 1,3-/1,2-migration-benzannulation cascade of propargylic esters **1** into naphthalenes **2** (eq 2).




Considering the enhanced electrophilicity of the $sp^3$ center[1b] in intermediate ***i***, we envisioned that incorporation

(1) For recent reviews, see: (a) Marco-Contelles, J.; Soriano, E. *Chem. Eur. J.* **2007**, *13*, 1350. (b) Marion, N.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2750.

(2) For recent reviews, 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) Echavarren, A. M.; Nevado, C. *Chem. Soc. Rev.* **2004**, *33*, 431. (e) Dyker, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 4237. (f) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180. (g) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896. (h) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410. (i) Yamamoto, Y. *J. Org. Chem.* **2007**, *72*, 7817. (j) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271. (k) Widenhoefer, R. A.; Han, X. *Eur. J. Org. Chem.* **2006**, 4555. (l) Ishida, T.; Haruta, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 7154. (m) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395.

(3) (a) Amijs, C. H. M.; López-Carrillo, V.; Echavarren, A. M. *Org. Lett.* **2007**, *9*, 4021. (b) Yu, M.; Zhang, G.; Zhang, L. *Org. Lett.* **2007**, *9*, 2147. (c) Wang, S.; Zhang, L. *J. Am. Chem. Soc.* **2006**, *128*, 8414. (d) Wang, S.; Zhang, L. *Org. Lett.* **2006**, *8*, 4585.

(4) (a) Lemière, G.; Gandon, V.; Cariou, K.; Fukuyama, T.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. *Org. Lett.* **2007**, *9*, 2207. (b) Buzas, A.; Gagosz, F. *J. Am. Chem. Soc.* **2006**, *128*, 12614. (c) Marion, N.; Díez-González, S.; Frémont, P.; Noble, A. R.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2006**, *45*, 3647. (d) Zhang, L.; Wang, S. *J. Am. Chem. Soc.* **2006**, *128*, 1442.

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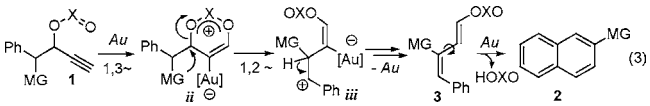
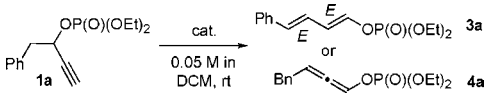
of a suitable 1,2-migrating group (MG) in ***ii*** would provoke a subsequent 1,2-shift[6] into ***iii***, which upon proton loss and protiodeauration would afford 1,3-diene[7] **3**. It is reasonable to propose that the latter may undergo 6$\pi$-electrocyclization into naphthalene[8,9] **2**, analogously to the known cyclization of acyloxy-1,3,5-trienes[10] (eq 3).




To this end, a possible isomerization of propargyl phosphate **1a** (MG = H) in the presence of different catalysts has been tested (Table 1). It was found that employment of

**Table 1.** Optimization of Reaction Conditions

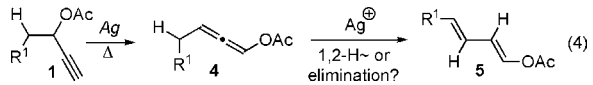



| entry | catalyst | yield **4a**, %[a] | yield **3a**, %[a] |
|---|---|---|---|
| 1 | 10% AgOTf | 73 | 0 |
| 2 | 5% $Ph_3PAuCl$, 5% AgOTf | 0 | 0 |
| 3 | 5% $AuCl_3$ | 0 | 0 |
| 4 | 5% $AuCl_3$, 15% AgOTf | 0 | 86 |
| 5 | 5% AuI | 0 | 86 |
| 6 | 5% $R_3PAuCl$ (R = Et, Ph) | 0 | 86 |

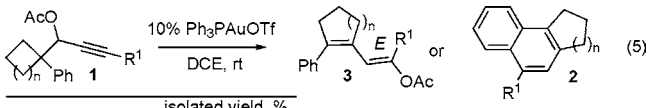
[a] Isolated yield of product for reaction performed on 0.1−0.2 mmol scale.

Ag triflate gave corresponding allene **4a** in good yield (entry 1). Remarkably, switching to cationic Au(I) triflate led to the formation of target 1,3-diene **3a** in 86% yield (entry 2). Monitoring of the reaction course revealed that this transformation proceeded through allenic intermediate **3a**.[12] Employment of Au(III) complexes (entries 3 and 4), noncationic Au(I) halides (entries 5 and 6), Cu(I) and Cu(II) triflates, as well as Brønsted or Lewis acids, resulted in no reaction.[12]

It deserves mentioning that the isomerization of acetates **1** into 1,3-dienes **5** in the presence of Ag-catalysts was reported (eq 4).[11] However, the nature of the second step (1,2-H-shift or proton elimination) remained unclear. To address this issue, we performed mechanistic studies[12] for MG = H (eq 3) employing Au(I) catalyst. Experiments revealed that the reaction proceeds exclusively via a 1,3-shift[13−15] −elimination[16] sequence.




Thus, we hypothesized that successful incorporation of a 1,2-migration into this cascade can only be achieved when a migrating group resides at a "proton-free" quaternary C-4 center. Therefore, isomerization of acetate **1d**, possessing a strained cyclobutane ring, was examined. Indeed, a tandem 1,3-migration and ring expansion via a 1,2-shift occurred leading to 1,3-diene **3d** in a moderate yield (eq 5). Moreover, isomerization of cyclopentyl homologs **1e** and **1f** afforded target naphthalenes **3e** and **3f** respectively (eq 5), thus providing a proof of concept for this cascade transformation.[17]




| | n | $R^1$ | isolated yield, % 3 | 2 |
|---|---|---|---|---|
| **d:** | 1 | H | 54 | - |
| **e:** | 2 | H | - | 36 |
| **f:** | 2 | *n*-Hex | - | 30 |

Next, cycloisomerization of substrates possessing better 1,2-migrating groups was examined (Table 2). Thus, a tandem acyloxy- or phosphatyloxy- and Ph-group migration/benzannulation of propargylic esters **1g**−**n** proceeded smoothly

(5) (a) Buzas, A.; Istrate, F.; Gagosz, F. *Org. Lett.* **2006**, *8*, 1957. (b) Zhang, L. *J. Am. Chem. Soc.* **2005**, *127*, 16804. (c) Luo, T.; Schreiber, S. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 8250. (d) Schwier, T.; Sromek, A. W.; Yap, D. M. L.; Chernyak, D.; Gevorgyan, V. *J. Am. Chem. Soc.* **2007**, *129*, 9868.

(6) For general review, see: (a) Ducrot, P. H. In *One or More CH and/or CC Bond(s) Formed by Rearrangement*; Katritzky, A. R., Taylor, R. J. K., Eds.; Comprehensive Organic Functional Group Transformations II; Elsevier: Oxford, UK, 2005; 1, pp 375−426.

(7) For syntheses of 1,3-dienes employing Au catalysis, see: (a) Buzas, A.; Istrate, F.; Gagosz, F. *Org. Lett.* **2007**, *9*, 985. (b) See also ref 3d.

(8) For a recent review on naphthalene syntheses, see: de Koning, C. B.; Rousseau, A. L.; van Otterlo, W. A. L. *Tetrahedron* **2003**, *59*, 7.

(9) For selected examples, see: (a) Dyker, G.; Hilderbrandt, D.; Liu, J.; Merz, K. *Angew. Chem., Int. Ed.* **2003**, *42*, 4399. (b) Zhao, J.; Hughes, C. O.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 7436. (c) Asao, N.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12650. See also: (d) Grisé, C. M.; Barriault, L. *Org. Lett.* **2006**, *8*, 5905. (e) Asao, N.; Sato, K. *Org. Lett.* **2006**, *8*, 5361. (f) Wang, S.; Zhang, L. *J. Am. Chem. Soc.* **2006**, *128*, 14274.

(10) Hamura, T.; Morita, M.; Matsumoto, T.; Suzuki, K. *Tetrahedron Lett.* **2003**, *44*, 167 and references therein.

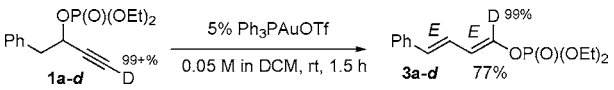
(11) (a) Saucy, G.; Marbet, R.; Lindlar, H.; Isler, O. *Helv. Chim. Acta* **1959**, *42*, 1945. (b) Schlossarczyk, H.; Sieber, W.; Hesse, M.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1973**, *56*, 875. (c) Cookson, R. C.; Cramp, M. C.; Parsons, P. J. *J. Chem. Soc., Chem. Comm.* **1980**, 197.

(12) See Supporting Information for details.

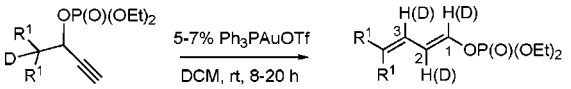
(13) Direct observation of the allenes **4** supported 1,3-migration path.[12]

(14) For reviews, see: (a) Allin, S. M.; Baird, R. D. *Curr. Org. Chem.* **2001**, *5*, 395. (b) Nubbemeyer, U. *Synthesis* **2003**, *7*, 961. (c) Fanning, K. N.; Jamieson, A. G.; Sutherland, A. *Curr. Org. Chem.* **2006**, *10*, 1007.

(15) D-Labeling studies on isomerization of **1a-*d*** ruled out possible involvement of alkyne-vinylidene isomerization path.



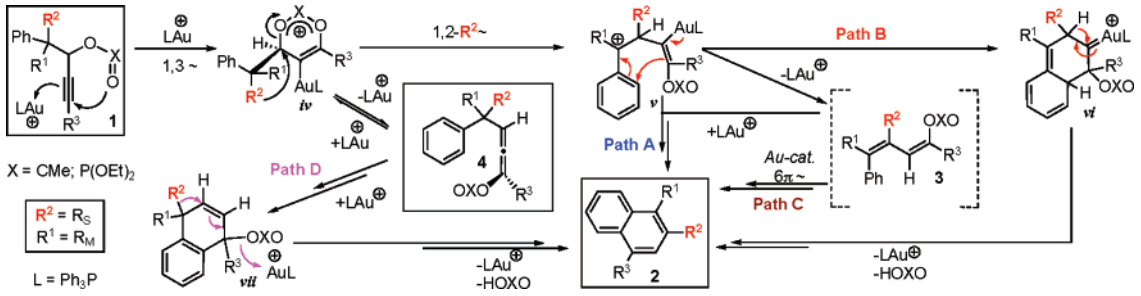

(16) Significant loss of D-label, as well as scrambling of the latter between C-1 and C-2, was observed for labeled phosphates **1b-*d*** and **1c-*d***. Reversible protonation at C-1 under the prolonged reaction times is most likely the reason for the observed notable incorporation of D at C-1.




| | | $d_1$-% | $d_2$-% | $d_3$-% | yield | |
|---|---|---|---|---|---|---|
| **1b-*d***: | $R^1$ = Me; 93% D | 27 | 21 | <2 | 65% | **3b-*d*$_n$** |
| **1c-*d***: | $R^1$ = Ph; 77% D | 10 | 33 | 0 | 64% | **3c-*d*$_n$** |

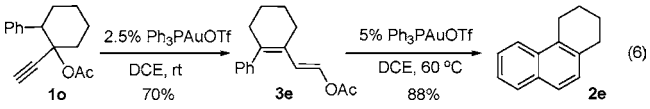
(17) For reasons, which are not clearly understood, **3d** did not cyclize into **2** even under forcing reaction conditions.

**Scheme 1.** Mechanistic Rationale for Au(I)-Catalyzed Cascade




to provide naphthalenes **2g**−**n** in good to excellent yields. Terminal, alkyl-, and aryl-substituted acetylenes were nearly equally efficient in this transformation. Unexpectedly, cyclization of dimethylphenyl-substituted acetate **1k** proceeded via exclusive 1,2-Me-group migration to give **3k** in good yield (entry 5). Notably, a variety of substituents, such as methoxy (entry 6), trifluoromethyl (entry 7), and 2-furyl (entry 8), were perfectly tolerated under these reaction conditions.

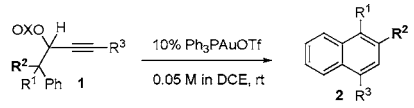
We propose the following plausible mechanisms for this novel cascade transformation (Scheme 1). Au-catalyzed 1,3-migration transforms **1** via cyclic intermediate[1b,3c,5b] ***iv*** into allene **4**.[13] According to path **A**, 1,2-alkyl migration[18] in ***iv*** produces benzylic cation ***v***. The latter gives diene **3** upon protiodeauration or after proton transfer undergoes Friedel−Crafts alkylation to furnish naphthalene **2**. Alternatively, a direct nucleophilic attack of vinyl-Au at the delocalized benzyl cation in ***v***[19] gives carbenoid intermediate ***vi***, which upon 1,2-H-shift[20] and aromatization produces naphthalene **2** (Path **B**).[21] According to path **C**, Au-catalyzed 6$\pi$-electrocyclization[14c,22] of **3** followed by elimination furnishes **2**. In another scenario, direct intramolecular hydroarylation of **4** followed by 1,2-shift and proton loss in ***vii*** produces **2** (Path **D**). Unexpected exclusive Me- over Ph-migration in **1k** is reasonably rationalized by stereoelectronic effect, according to which Ph group cannot accommodate requisite antiperiplanar orientation with the leaving group in ***iv***.[12,23,24] Successful cycloisomerization of **3e**, obtained via 1,3-migration/elimination cascade, into naphthalene **2e** provided an additional support for possible intermediacy of 1,3-dienes in this transformation (eq 6).

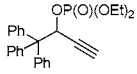
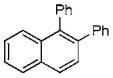
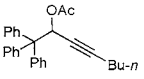
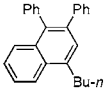
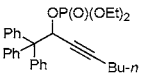
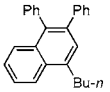
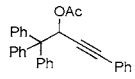
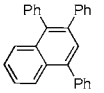
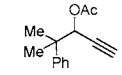
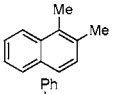
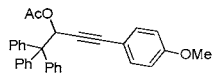
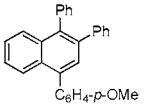
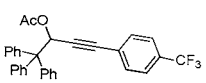
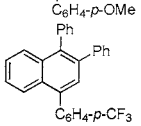
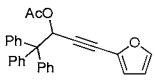
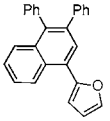



(6)

In summary, we have developed a novel gold(I)-catalyzed approach toward polysubstituted naphthalenes, which features an unprecedented tandem sequence of 1,3- and 1,2-migration

**Table 2.** Gold(I)-Catalyzed Synthesis of Naphthalenes




| entry | substrate | product | | yield, %[a,b] |
|---|---|---|---|---|
| 1 |  |  | **2g** | 86[c] |
| 2 |  |  | **2h** | 94 |
| 3 |  |  | **2h** | 50 |
| 4 |  |  | **2j** | 75 |
| 5 |  |  | **2k** | 73 |
| 6 |  |  | **2l** | 90 |
| 7 |  |  | **2m** | 84 |
| 8 |  |  | **2n** | 94 |

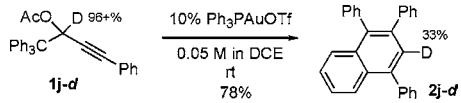
[a] Isolated yield. [b] Reactions were performed on a 0.5 mmol scale. [c] 5% Au-catalyst was used.

(18) For selected examples, see: (a) Dudnik, A. S.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2007**, *46*, 5195. (b) Kirsch, S. F.; Binder, J. T.; Liébert, C.; Menz, H. *Angew. Chem., Int. Ed.* **2006**, *45*, 5878.

(19) See, for example: (a) Luzung, M. R.; Mauleón, P.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 12402. (b) See also ref 4a,b.

(20) For selected examples, see: (a) Markham, J. P.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 9708. (b) Gorin, D. J.; Davis, N. R.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 11260. (c) Sromek, A. W.; Rubina, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2005**, *127*, 10500.

(21) Path **B** involving clean 1,2-H-shift to Au-carbenoid is not supported by the observed significant loss of D-label in cycloisomerization of **1j-*d***.




(22) See also: Menz, H.; Kirsch, S. F. *Org. Lett.* **2006**, *8*, 4795.

(23) For similar considerations, see: Aggarwal, V. K.; Sheldon, C. G.; Macdonald, G. J.; Martin, W. P. *J. Am. Chem. Soc.* **2002**, *124*, 10300.

of different migrating groups in propargylic esters. A more detailed investigation on the mechanism, as well as the scope of this cascade, is ongoing and will be reported in due course.

(24) Obviously, exclusive Me- vs Ph-migration can also be explained via Path **D**, according to which 1,2-migration occurs after cyclization step. Alternatively, as proposed by the reviewer, migration of the Me group leading to the more stable intermediate benzylic carbocation under thermodynamic control can also account for the observed chemoselectivity.

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**Supporting Information Available:** Preparative procedures and analytical and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

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