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Gold(I)-Catalyzed Isomerization of Allenyl Carbinol Esters: An Efficient Access to Functionalized 1,3-Butadien-2-ol Esters

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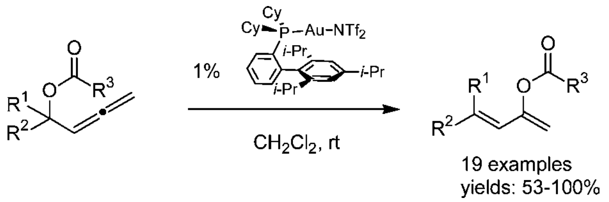
ABSTRACT



A study concerning the gold(I)-catalyzed rearrangement of diversely substituted allenyl carbinol esters into functionalized 1,3-butadien-2-ol esters is described. The mild conditions employed allow the efficient, rapid, and stereoselective synthesis of a variety of such compounds via a new 1,3-shift of an ester moiety onto a gold-activated allene.

Functionalized 1,3-butadien-2-ol esters are attractive building blocks in organic synthesis. They have been sucessfully employed in a range of transformations mostly as diene units for inter-[1] or intramolecular[2] Diels−Alder reactions but also in [4+1] cycloadditions,[3] in metal-catalyzed addition reactions,[4] and in stereoselective hydrogenation reactions for the synthesis of chiral allylic esters.[5] Surprisingly, there are only a few methods to access such dienes and most of them use enones as starting material and involve either high temperature[6] or strong basic[7] or acidic conditions[8] which are not always compatible with the substitution pattern of the substrates.

Gold(I) complexes have emerged as efficient and mild catalysts[9] for the transformation of substrates possessing either an alkyne[10] or an allene[11] functionality into a range of useful structural motifs. As part of a program directed toward the development of new gold-catalyzed reactions,[12] we discovered and now report that allenyl carbinol esters could be efficiently and stereoselectively isomerized into the corresponding 1,3-butadien-2-ol esters using a catalytic amount of a gold(I) catalyst.[13]

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(1) For examples, see: (a) Danishefsky, S.; Kahn, M. *Tetrahedron Lett.* **1981**, *22*, 489−492. (b) Areces, P.; Jimenez, J. L.; Pozo, M. C.; Roman, E.; Serrano, J. A. *J. Chem. Soc., Perkin Trans. 1* **2001**, 7754−762. (c) Kresze, G.; Haertner, H. *Justus Liebigs Ann. Chem.* **1973**, 650−658.

(2) For examples, see: (a) Pollini, G. P.; Bianchi, A.; Casolari, A.; Risi, C.; Zanirato, V.; Bertolasi, V. *Tetrahedron: Asymmetry* **2004**, *15*, 3223−3232. (b) Katsumura, S.; Kimura, A.; Isoe, S. *Tetrahedron* **1989**, *45*, 1337−1346.

(3) Roversi, E.; Vogel, P. *Helv. Chim. Acta* **2002**, *85*, 761−771.

(4) (a) Kosugi, M.; Hagiwara, I.; Sumiya, T.; Migita, T. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 241−246. (b) Allard, M.; Levisalles, J. *Bull. Soc. Chim. Fr.* **1972**, 1926−1931. (c) Larock, R. C.; Song, H. *Synth. Commun.* **1989**, *19*, 1463−1470. (d) Novak, L.; Rohaly, J.; Kolonits, P.; Fekete, J.; Varjas, L.; Szantay, C. *Liebigs Ann. Chem.* **1982**, 1173−1182.

(5) Boaz, N. W. *Tetrahedron Lett.* **1998**, *39*, 5505−5508.

(6) Kalita, B.; Bezbarua, M. S.; Barua, N. C. *Synth. Commun.* **2002**, *32*, 3181−3184.

(7) Seltzer, S. *J. Org. Chem.* **1995**, *60*, 1189−1194.

(8) Potman, R. P.; Kleef, F. J.; Scheeren, H. W. *J. Org. Chem.* **1985**, *50*, 1955−1959.

(9) For recent reviews, see: (a) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271−2296. (b) Ma, S.; Yu, S.; Gu, Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 200−203. (c) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2005**, *44*, 6990−6993. (d) Hoffmann-Roder, A.; Krause, N. *Org. Biomol. Chem.* **2005**, *3*, 387−391.

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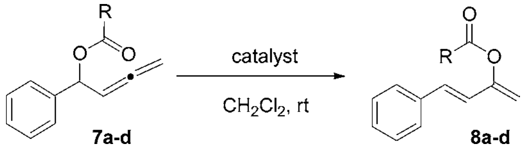
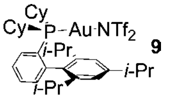
Table 1. Optimization of the Catalytic System[a]

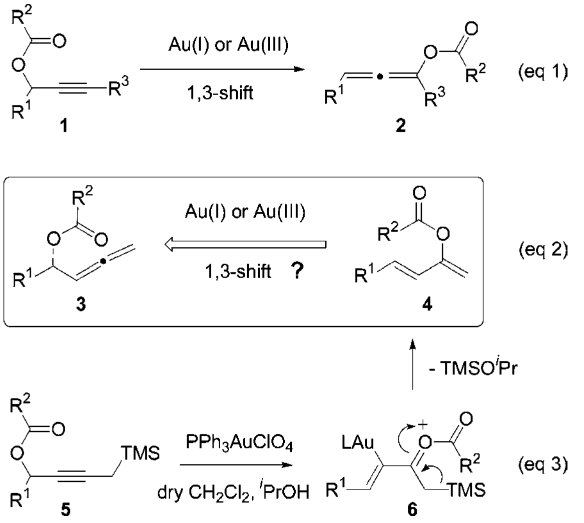


entry	R	substrate	catalyst	time	conversion[b]		yield
1	Me	**7a**	$AuBr_3$, 2 mol %	24 h	<5%	**8a**	0%
2	Me	**7a**	$AgNTf_2$, 10 mol %	24 h	15%	**8a**	6%[b]
3	Me	**7a**	PPh_3AuNTf_2, 1 mol %	24 h	15%	**8a**	14%[b]
4	Me	**7a**	 1 mol %	3 h	100%	**8a**	98%[c]
5	Bz	**7b**	1 mol %	75 min	100%	**8b**	100%[c]
6	C(Me)$_3$	**7c**		45 min	100%	**8c**	100%[c]
7	O^{t}Bu	**7d**		20 h	75%	**8d**	69%[c]

[a] Reaction conditions: 0.25 M substrate in CH_2Cl_2. [b] Estimated by ^1H NMR. [c] Isolated yield.

The gold-catalyzed isomerization of propargylic esters **1** to carboxyallenes **2** has been recently used in various tandem processes leading to a range of synthetically important products (eq 1, Scheme 1).[14] By analogy with this transformation and given the capability of gold complexes to activate allenes,[11] we envisioned that allenyl carbinol esters such as **3** might be valuable precursors for the synthesis of 1,3-butadien-2-ol esters (e.g., **4**) after an analogous gold-catalyzed 1,3-shift of the ester functionality (eq 2). Interestingly, Wang and Zhang have recently reported a new gold(I)-catalyzed reaction for the formation of such 1,3-butadien-2-ol esters **4** from trimethylsilylmethyl-substituted propargyl ester **5**.[15] This tandem transformation proceeds through the initial generation of the oxocarbenium intermediate **6** followed by desilylation and subsequent protodemetalation of the vinyl gold species (eq 3).

Scheme 1. Synthetic Approach to Functionalized 1,3-Butadien-2-ol Esters



Even if this reaction proved to be efficient (54−87% yield) and led to the corresponding diene derivatives with an excellent *E*-selectivity, we believed that our approach could present some advantages. The required allenic substrates **3** could

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(10) For selected recent examples, see: (a) Gorin, D. J.; Dube, P.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 14480−14481. (b) López, S.; Herrero-Gómez, E.; Pérez-Galán, P.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 6029−6032. (c) Toullec, P. Y.; Genin, E.; Leseurre, L.; Genêt, J.-P.; Michelet, V. *Angew. Chem., Int. Ed.* **2006**, *45*, 7427−7430. (d) Wang, S.; Zhang, L. *J. Am. Chem. Soc.* **2006**, *128*, 14274−14275. (e) Sun, J.; Conley, M. P.; Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2006**, *128*, 9705−9710. (f) Kirsch, S. F.; Binder, J. T.; Liébert, C.; Menz, H. *Angew. Chem., Int. Ed.* **2006**, *45*, 5878−5880. (g) Lemière, G.; Gandon, V.; Agenet, N.; Goddard, J.-P.; De Kozak, A.; Aubert, C.; Fensterbank, L.; Malacria, M. *Angew. Chem., Int. Ed.* **2006**, *45*, 5796−5799.

(11) For selected recent examples, see: (a) Gockel, B.; Krause, N. *Org. Lett.* **2006**, *8*, 4485−4488. (b) Zhang, Z.; Liu, C.; Kinder, R. E.; Han, X.; Qian, H.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2006**, *128*, 9066−9073. (c) Nishina, N.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 3314−3317. (d) Morita, N.; Krause, N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1897−1899.

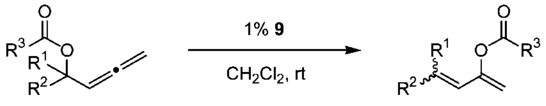
(12) (a) Buzas, A.; Gagosz, F. *J. Am. Chem. Soc.* **2006**, *128*, 12614−12615. (b) Buzas, A.; Gagosz, F. *Synlett* **2006**, 2727−2730. (c) Buzas, A.; Istrate, F.; Gagosz, F. *Org. Lett.* **2006**, *8*, 1957−1959. (d) Buzas, A.; Gagosz, F. *Org. Lett.* **2006**, *8*, 515−518.

(13) For related studies dealing with the acid-catalyzed or thermal rearrangement of allenyl carbinol esters into 1,3-butadien-2-ol esters, see: (a) Olsson, L. I.; Claesson, A.; Bogentof, C. *Acta Chem. Scand.* **1973**, *27*, 1629−1636. (b) Horvath, A.; Bäckvall, J.-E. *J. Org. Chem.* **2001**, *66*, 8120−8126. (c) Bridges, A. J.; Thomas, R. D. *Chem. Commun.* **1983**, 485−486.

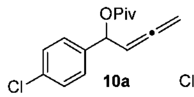
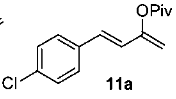
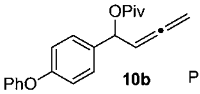
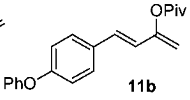
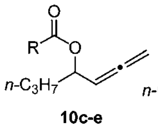
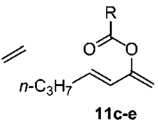
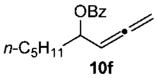
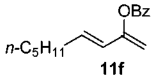
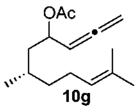
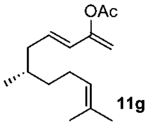
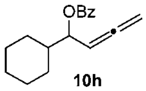
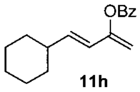
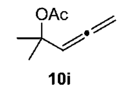
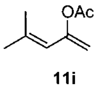
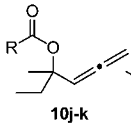
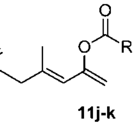
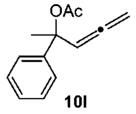
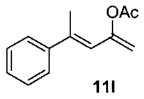
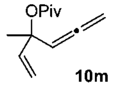
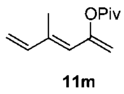
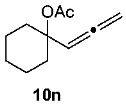
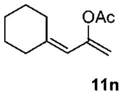
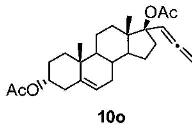
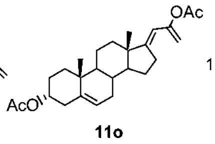
(14) For selected examples, see: (a) Zhao, J.; Hughes, C. O.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 7436−7437. (b) Wang, S.; Zhang, L. *J. Am. Chem. Soc.* **2006**, *128*, 8414−8415. (c) Wang, S.; Zhang, L. *J. Am. Chem. Soc.* **2006**, *128*, 1442−1443. (d) Zhang, L. *J. Am. Chem. Soc.* **2005**, *127*, 16804−16805.

(15) Wang, S.; Zhang, L. *Org. Lett.* **2006**, *8*, 4585−4587.

Table 2. Isomerizations of Various 4-Substituted 1,2-Butadien-4-ol Esters[a]



10a-n → **11a-o**

entry	substrate	product	time	yield (Z:E)[b]
1	 **10a**	 **11a**	2 h	100% (1:18)
2	 **10b**	 **11b**	8 h	78% (1:8)
3	 **10c-e**	 **11c-e**	R= Me **11c** 3 h R= CMe$_3$ **11d** 1 h R= Bz **11e** 5 min	100% (1:7) 100% (1:9) 100% (1:19)
4	 **10f**	 **11f**	40 min	100% (1:15)
5	 **10g**	 **11g**	2 h	99% (1:8)
6	 **10h**	 **11h**	9 h	100% (0:1)
7	 **10i**	 **11i**	5 min	100% [e]
8	 **10j-k**	 **11j-k**	R= Me **11j** 5 min R= CMe$_3$ **11k** 5 min	79% (100%)[d] (1:1.7) 67% (89%)[d,f] (1:1.4)
9	 **10l**	 **11l**	3 h	59% (1:1) [c]
10	 **10m**	 **11m**	10 min	53% (93%)[d] (1:2)
11	 **10n**	 **11n**	5 min	100%
12	 **10o**	 **11o**	1 h	97% (1:10)

[a] Reaction conditions: 0.25 M enyne in DCM with 1 mol % of **9**. [b] Ratio determined by ^{1}H NMR. [c] Reaction performed in refluxing 1,2-dichloroethane. Diene **11l** was isolated in the mixture with the unreacted allene **10l**. [d] Yield determined by ^{1}H NMR on the crude reaction mixture. [e] Reaction performed in an NMR tube. Yield determined by ^{1}H NMR on the crude reaction mixture. [f] Reaction performed at 0 °C.

indeed be easily obtained by a Crabbé homologation of acetylenes to allenes using less expensive starting material than propargyltrimethylsilane. Moreover, the use of dry dichloromethane would not be required because no water-sensitive intermediate acyloxocarbenium species **6** would be involved.

Allene **7a** was first chosen as a model substrate to validate our approach (Table 1). Reacting this substrate with 2 mol % of AuBr$_3$ at room temperature in dichloromethane led to a poor conversion of **7a** with no formation of the desired diene **8a** (entry 1). The use of a silver salt as the catalyst did not really improve the conversion, but diene **8a** could however be isolated in a poor 6% yield (entry 2).[16] Following our recent success in using the crystalline, air-stable PPh$_3$AuNTf$_2$ catalyst for the formation of C−O bonds,[12b−d] we attempted to use this catalytic system to improve the yield of **8a**. However, in the presence of 1 mol % of PPh$_3$AuNTf$_2$, only 14% of the desired compound could be obtained (entry 3). We therefore turned our attention to the use of biphenylphosphine-based catalysts. Remarkably, the use of 1 mol % of catalyst **9**[17] dramatically improved the isomerization, and diene **8a** was isolated in an excellent 98% yield as a single *E*-isomer (entry 4). It is worth noting that enol acetate **8a** could not be obtained using the procedure developed by Wang and Zhang.[15] Besides acetates, other ester groups underwent this 1,3-shift. Benzoate **7b** and pivalate **7c** quantitatively furnished the corresponding dienes **8b** and **8c** in a reduced reaction time (entries 5 and 6). *Tert*-butyl carbonate **7d** reacted more slowly and furnished diene **8d** in 65% yield (entry 7). It is interesting to note that no fragmentation of the Boc group, which would lead to an *exo*-methylene dioxolanone, was observed.[12d] In light of these results, catalyst **9** was retained in the study of the scope of this transformation.

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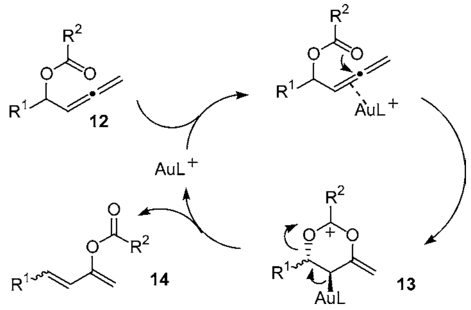
[16] Poor conversions or low yields were obtained when the rearrangement of **7b** was performed under acidic conditions[13a,b] (10 mol % of HNTf$_2$ in CH$_2$Cl$_2$ at rt for 24 h: no conversion) or thermal conditions[13c] (in refluxing toluene for 24 h: <5% yield).

[17] Mezailles, N.; Ricard, L.; Gagosz, F. *Org. Lett.* **2005**, *7*, 4133−4136.

Scheme 2. Mechanistic Proposal for the Isomerization

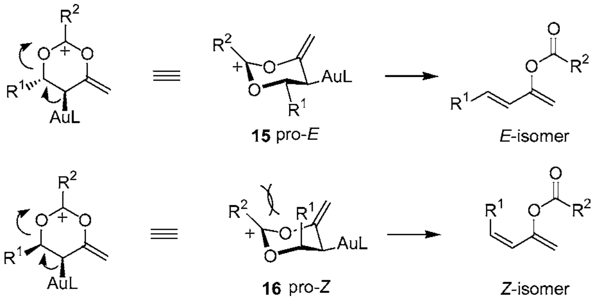


The reaction proved to be quite general, and various allenyl carbinol esters **10a**−**o** reacted using 1 mol % of **9** as the catalyst to furnish the corresponding dienes **11a**−**o** in generally good yields (53−100%) and *E*-selectivities (Table 2). The time required to reach completion was in most cases shorter than 2 h. Other aryl-substituted substrates were tolerated even if a slight decrease in yield was observed in the case of the *p*-phenoxy-substituted allene **10b** (entries 1 and 2). The transformation was not limited to use of aryl-substituted allenes, as demonstrated by the examples presented in entries 3−6. A sterically demanding substituent at the α-allenic position was tolerated, and enol benzoate **11h** was isolated in quantitative yield (entry 6). An interesting effect of the nature of the migrating ester group on the stereoselectivity of the reaction was observed in the cases of allenes **10c**−**e** (entry 3). Even if such an effect is difficult to rationalize at this point of the study, the formation of the *E*-isomer seems to be favored by the use of a benzoate as the migrating group. The *Z*/*E* ratio increases up to 1:19 in the case of a benzoate (entries 3, 4, and 6), and the use of an acetate or a pivalate generally leads to a *Z*/*E* ratio of around 1:8.[18] The isomerization was not limited to the use of allenes monosubstituted at the α-position, and tertiary substrates **10i**−**o** reacted equally well, even if a decrease in selectivity was observed (entries 7−12). The reaction of androstene derivative **10o** was exceptionally efficient and gave the corresponding enol acetate **11o** in 97% yield after a simple filtration of the crude reaction mixture (entry 12). Surprisingly, the isomerization of allene **10l** could not be performed in dichloromethane, and refluxing for 3 h in 1,2-dichloroethane was required to furnish diene **11l**, which was isolated in a modest 59% yield along with unreacted substrate **10l**. Finally, it is worth noting that, besides dienes, trienes could also be synthesized using this method as demonstrated by the example presented in entry 10.

On the basis of these observations, a mechanistic manifold for the formation of the dienes is presented in Scheme 2. Regioselective gold(I) activation of the allene in **12** promotes the nucleophilic attack of the carbonyl function of the ester moiety and the subsequent formation of the stabilized cationic species **13**. Simultaneous fragmentation of the homoallylic C−O bond and the allylic Au−C bond in **13** leads to the 1,3-shift of the ester group with formation of diene **14** and regeneration of the gold catalyst.[19]

The stereoselectivity observed in the reaction may be explained by considering the two possible half-chair transition states **15** and **16** leading, respectively, to the formation of the *E* and *Z* isomers (Scheme 3). In the pro-*E* transition state **15**, the R^1 substituent and the gold atom adopt a preferential pseudoequatorial position with the requisite antiperiplanar relationship between the homoallylic C−O bond and the allylic Au−C bond. At the opposite, in the pro-*Z* transition state **16**, the R^1 group adopts an energetically less-favored pseudoaxial position leading to possible 1,3 diaxial interactions whereas the gold atom remains in a pseudoequatorial position.

Scheme 3. Source of the *E*/*Z* Selectivity



In summary, we have developed a new efficient method for the synthesis of functionalized 1,3-butadien-2-ol esters from readily available allenyl carbinol esters. The reaction conditions are mild; the loading of the catalyst is low; and the *E*-selectivity is generally good. Further studies related to the gold-catalyzed isomerization of polysubstituted allenes as well as studies to rationalize the influence of the nature of the ester on the *E*-selectivity are underway and will be reported in due course.

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

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[18] It was proven that gold catalyst **9** did not isomerize the final dienes because performing the isomerization for a longer time or resubmitting the isolated dienes to the same reaction conditions did not change the *Z*/*E* ratios.

[19] An alternative mechanism involving the activation of the terminal double bond of the allene moiety may be envisaged.