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Gold-Catalyzed Efficient Formation of Alkenyl Enol Esters/Carbonates from Trimethylsilylmethyl-Substituted Propargyl Esters/Carbonates

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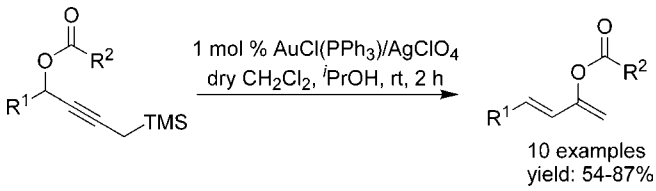
ABSTRACT



A gold-catalyzed efficient method for the preparation of alkenyl enol esters/carbonates is developed. Besides the mild reaction conditions and high catalytic efficiency, the excellent *E*-selectivity of the nonenolic double bond is remarkable.

Alkenyl enol esters/carbonates are versatile synthons in organic synthesis, readily engaging in a range of transformations including regioselective Diels−Alder reactions,[1] stereoselective hydrogenation into chiral allylic esters,[2] and Pd-catalyzed enantioselective allylation.[3] They are generally prepared from the corresponding enones at elevated temperatures[4] or under strong basic or acidic conditions, thus raising the issue of functional group compatibility.

Recent revelation of the exceptional capability of Au salts/complexes[5] in the activation of alkynes,[6] allenes,[7] and alkenes[8] has led to a rapid increase of Au-catalyzed preparative methods for various synthetic intermediates. In our continuing effort in discovering synthetic potentials of propargylic esters in the presence of a Au catalyst,[9] we discovered and herein reported an efficient preparative method of alkenyl enol esters/carbonates from trimethylsilylmethyl-substituted propargylic esters/carbonates. Moreover, high *E*-selectivities are observed in the nonenolic C−C double bond of the products.

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

(5) For 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-Roder, A.; Krause, N. *Org. Biomol. Chem.* **2005**, *3*, 387. (d) Arcadi, A.; Di Giuseppe, S. *Curr. Org. Chem.* **2004**, *8*, 795. (e) Arcadi, A.; Di Giuseppe, S.; Marinelli, F.; Rossi, E. *Adv. Synth. Catal.* **2001**, *343*, 443. (f) Echavarren, A. M.; Nevado, C. *Chem. Soc. Rev.* **2004**, *33*, 431. (g) Hashmi, A. S. K. *Gold Bull.* **2003**, *36*, 3. (h) Dyker, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 4237.

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We have previously shown that in the presence of either cationic $[Au(PPh_3)]^+SbF_6^-$ or dichloro(pyridine-2-carboxylato)Au(III) propargylic esters were converted into a range of synthetically important products, including α-ylidene-β-diketones,[9a] cyclopentenones,[9b] and 2,3-indoline-fused highly functionalized cyclobutanes.[9c] All these reactions can be explained by the existence of a common reactive Au-containing alkenyl acyloxocarbenium intermediate, formed via tandem Au-catalyzed 3,3-rearrangement of propargylic esters and activation of the in situ generated carboxyallenes. In line with this rationale, we surmised that trimethylsilylmethyl-substituted propargyl ester **1**, readily available from propargyltrimethylsilane and aldehydes, could undergo a similar tandem process (Figure 1), leading to oxocarbenium

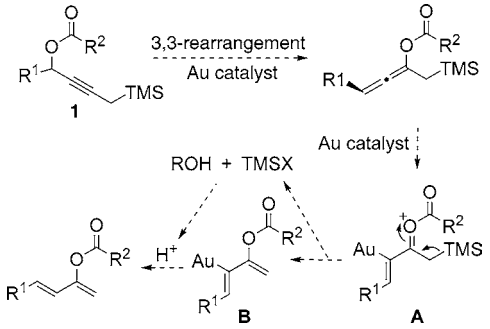
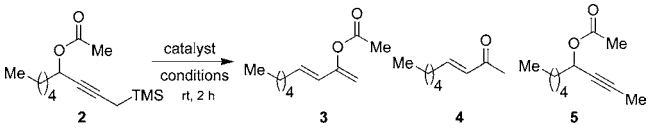


Figure 1. Au-catalyzed tandem process for alkenyl enol ester/carbonate formation.

intermediate **A** with a trimethylsilyl group α to the electrodeficient carbonyl carbon center. It was envisioned that a subsequent desilylation could happen readily and would result in a Au-containing alkenyl enol ester (i.e., **B**). In the presence of a proton source (H_2O or alcohol), the TMSX generated during desilylation can be converted into acid HX. Facile protonation of the Au−C(sp^2) bond will then yield alkenyl enol ester with concomitant regeneration of the Au catalyst.

We started by treating 1-trimethylsilyl-2-nonyn-4-yl acetate (**2**)[10] with 5 mol % of $AuCl_3$ in wet CH_2Cl_2 (Table 1, entry 1), and gratifyingly, the expected alkenyl enol acetate **3** was formed in 2 h, although in only 26% yield. The major side product was enone **4**, and a small amount of desilylation product **5** was also formed. Using the cationic Au(I) complex, $[AuPPh_3]^+ NTf_2^-$,[11] instead led to almost exclusive formation of **4**, and there was still a small amount of propargylic acetate **2** unreacted (entry 2). Surprisingly, 1 mol % of $[AuPPh_3]^+ ClO_4^-$[12] catalyzed complete conversion of **2** and, more importantly, a promising yield of **3** was formed (entry 3). To further improve this reaction, we tried other cationic Au-

Table 1. Optimization of Reaction Conditions[a]



entry	catalyst	conditions	conv. [%]	yield [%][b] 3	4	5
1	5 mol % of $AuCl_3$	wet CH_2Cl_2	75	26	43	2
2	1 mol % of $[Au(PPh_3)]^+ NTf_2^-$	wet CH_2Cl_2	81	<1	59	<1
3	1 mol % of $AuCl(PPh_3)$/$AgClO_4$	wet CH_2Cl_2	>99	50	42	7
4	1 mol % of LAuCl/$AgClO_4$[c]	wet CH_2Cl_2	>99	38	36	7
5	1 mol % of $AuCl[P(C_6F_5)_3]$/$AgClO_4$	wet CH_2Cl_2	>99	36	41	3
6	1 mol % of $AuCl(PPh_3)$/$AgClO_4$	dry CH_2Cl_2, ^{t}BuOH	>99	82[d]	7	7
7	1 mol % of $AuCl(PPh_3)$/$AgClO_4$	dry CH_2Cl_2, ^{i}PrOH	>99	84[d]	4	3

[a] The concentration of **2** is 0.05 M. [b] Estimated by ^{1}H NMR using 1,2,3,4-tetramethylbenzene as the internal standard. [c] L = 2-(dicyclohexylphosphino)biphenyl. [d] Isolated yield.

(I) catalysts albeit without much success (e.g., entries 4 and 5). Finally, we found that the proton source was critical for the selective formation of **3**. Hence, using ^{t}BuOH[13] (entry 6) instead of H_2O, we isolated enol acetate **3** in excellent yield (82%) with only a small amount of **4** and **5** formed. Even better selectivity was observed using ^{i}PrOH[14] as a proton source, and **3** was obtained in a slightly higher yield (entry 7).[15] Two noteworthy features of this initial result are the low catalyst loading (1 mol %) and the high stereoselectivity as only the *E*-isomer of **3** was observed.

With the optimized reaction conditions [1 mol % of $AuCl(PPh_3)/AgClO_4$, dry CH_2Cl_2, ^{i}PrOH], the scope of this reaction was then examined. As shown in Table 2, sterically demanding substituents at the propargylic position were tolerated, and alkenyl enol acetates **7a** and **7b** were isolated in good yields (entries 1 and 2). Although a phenyl group at the propargylic position led to a messy reaction, electron-deficient aryl groups gave much better results (e.g., entries 3−5). Noteworthy is the functional group compatibility as both an ester group and a bromo group were tolerated. Besides enol acetates, other alkenyl enol esters can be prepared smoothly. For example, both enol pivaloate **7f** and benzoate **7g** were formed in good to excellent yields (entries 6 and 7). Again, these reactions showed high catalytic efficiency and excellent stereoselectivity.

Remarkably, propargylic carbonates underwent similar transformations, and the corresponding *E*-alkenyl enol carbonates were efficiently formed. Hence, propargylic methyl carbonate **8** was a good substrate for the tandem 3,3-

(10) Acetate **2** and other substrates were prepared straightforwardly via reacting aldehydes with in situ-generated 3-trimethylsilyl-1-propyn-1-yllithium followed by conventional esterification/carbonation of the crude alcohols.

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

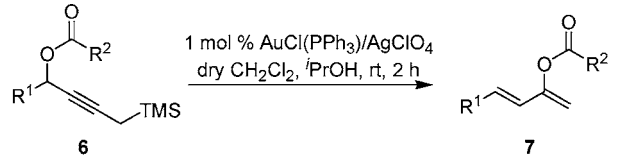
(12) The role of ClO_4^- is not known to us at this point.

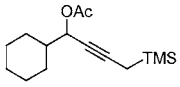
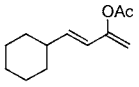
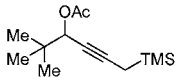
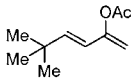
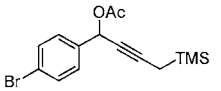
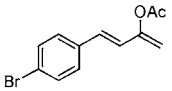
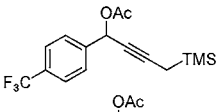
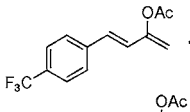
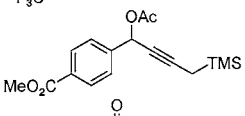
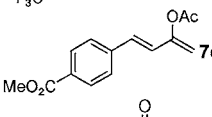
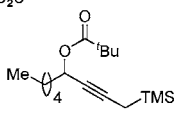
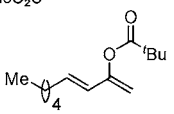
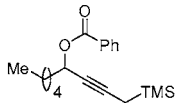
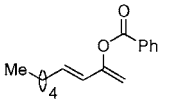
(13) ^{t}BuOH was used as solvent to dissolve $AgClO_4$ (0.05 M), which is only slightly soluble in CH_2Cl_2, and the solution containing 1 mol % of $AgClO_4$ was then added to the reaction. For details, see the experimental procedure.

(14) ^{i}PrOH was used similar to the case of ^{t}BuOH.

(15) The advantage of bulky alcohols over H_2O is likely due to hampered desilylation leading to propargyl acetate **5**. The side reaction might involve the assistance of a weak nucleophile such as H_2O or alcohols and is likely hindered by the steric bulkiness of ^{i}PrOH or ^{t}BuOH.

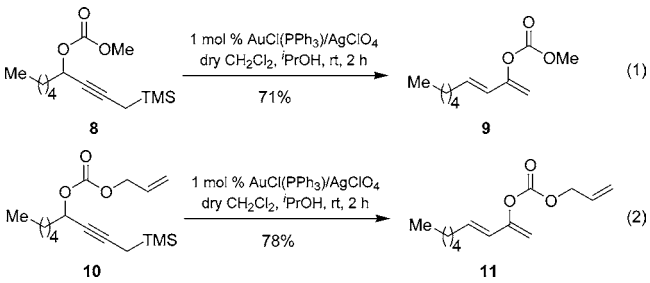
Table 2. Efficient Formation of Alkenyl Enol Esters



entry	6	7	yield [%][a]
1		 **7a**	82
2		 **7b**	76
3		 **7c**	54
4		 **7d**	87
5		 **7e**	86
6		 **7f**	65
7		 **7g**	80

[a] Yield based on excluding the inseparable desilylating side product according to ^{1}H NMR integration.

rearrangement and desilylation, leading to 71% of alkenyl enol carbonate **9** (eq 1). Interestingly, allyl carbonate **10** also worked well, and the corresponding product **11** was isolated



in good yield (eq 2). Noteworthy in this case is that the allyl C−C double bond did not interfere with the reaction.[16] In addition, compound **11** is a useful substrate for Pd-catalyzed decarboxylative allyl migration.[17]

In closing, we have developed an efficient method for the preparation of alkenyl enol esters/carbonates from readily accessible trimethylsilylmethyl-substituted propargyl esters/carbonates. Besides the mild reaction conditions and high catalytic efficiency, the high *E*-selectivity of the nonenolic double bond is remarkable. Further studies on expanding the scope of this reaction to include substrates derived from ketones and utilizing the nucleophilic Au−C(sp^2) bond will be pursued.

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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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(16) We have shown previously (see ref 6c) that electron-rich double bonds could cyclize intramolecularly to the oxocarbenium intermediate.

(17) For the original study, see: Tsuji, J.; Minami, I.; Shimizu, I. *Tetrahedron Lett.* **1983**, *24*, 1793. For asymmetric versions of this reaction, see ref 3.