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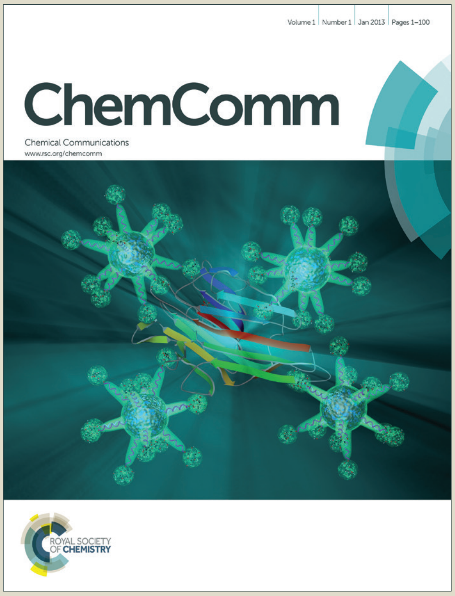

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Gold-catalyzed Reactions of Propargylic Esters with Vinylazides for the Synthesis of *Z*- or *E*-configured Buta-1,3-dien-2-yl esters

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Gold-catalyzed synthesis of buta-1,3-dien-2-yl esters from the reactions of propargyl esters and vinylazides are described; the reaction mechanism is postulated to involve a vinyl attack of vinylazides at alkenyl gold carbenes.

Buta-1,3-dien-2-yl esters are useful four-carbon building units in Diels-Alder reactions,[1] which are powerful tools to access complicated naturally occurring alkaloids.[2] These species serve also as reagents for the synthesis of monofluoroalkyl *α,β*-unsaturated ketones.[3] They are accessible also to various chiral molecules through asymmetric hydrogenations[4a] and enantio-selective allylation reaction.[4b] Convenient syntheses of buta-1,3-dien-2-yl esters rely on transition metal-catalyzed reactions including Au(I)-catalyzed rearrangement of propargylic esters[5] (eq 1) and gold and rhodium-catalyzed rearrangement of allenyl esters (eq 2).[6] Dixneuf et al. recently reported ruthenium-catalyzed reactions of propargylic esters with diazoalkanes to form buta-1,3-dien-2-yl esters (eq 3).[7] In this work, we report gold-catalyzed reactions of propargylic esters with vinylazides,[8] to form *Z*- or *E*-configured buta-1,3-dien-2-yl esters and nitriles. This process has mechanistic interest because the C=C bonds of vinylazides become cleaved with the resulting =CH_2 fragment adding to the terminal alkynyl carbons of propargyl esters. The control of the *Z* and *E* configurations of resulting buta-1,3-dien-2-yl esters is also discussed.

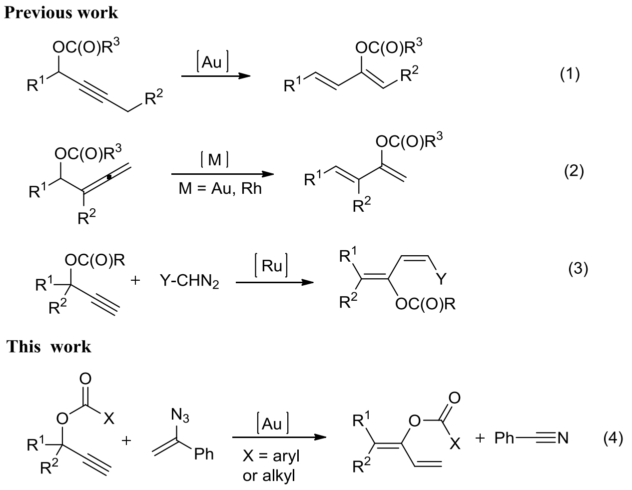
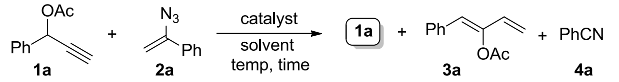


Table 1. Catalyst screening for the formation buta-1,3-dien-2-yl esters



Entry	Catalyst[c] (10 mol%)	Solvent	*t* (°C)	*t* (h)	yield (%)[a,b] 1a	3a	4a
1	$PPh_3AuCl/AgSbF_6$	DCE	80	22	33	45	nd
2	$LAuCl/AgSbF_6$	DCE	80	26	--	67	64
3	$IPrAuCl/AgSbF_6$	DCE	80	30	--	63	nd
4	$LAuCl/AgNTf_2$	DCE	80	24	29	52	nd
5	$LAuCl/AgSbF_6$	toluene	100	16	85	trace	nd
6	$LAuCl/AgSbF_6$	CH_3NO_2	90	14	83	trace	nd
7	$LAuCl/AgSbF_6$	THF	65	24	49	--	nd
8	$AgSbF_6$	DCE	80	25	95	--	nd

[a] **1a** (0.191 M, 1.0 equiv), **2a** (2.0 equiv), [b]Product yields are given after purification from a silica column, IPr = 1,3-bis(diisopropyl phenyl) imidazol-2-ylidene, L = P(*t*-Bu)$_2$(*o*-biphenyl), nd = not determined.

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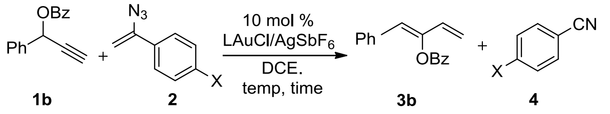
Table 1 shows the optimization of reactions between propargyl ester **1a** and vinylazide **2a** using various gold catalysts. Our test with various gold catalysts (entries 1-4) revealed that electron-rich and bulky LAuCl/$AgSbF_6$ [L = P(*t*-Bu)$_2$(*o*-biphenyl)] and IPrAuCl/$AgSbF_6$ (IPr = 1,3-bis(diisopropylphenyl)imidazole-2-ylidene) were efficient to yield buta-1,3-dien-2-yl ester **3a** in 67% and 63% yields respectively, with complete consumption of initial **1a**. We identified the presence of benzonitrile in entry 2 through GC-MS; its yield was estimated by ^{1}H NMR of crude products. Other solvents including toluene, nitromethane and THF, were all ineffective, giving product **3a** in negligible proportion (entries 5-7). $AgSbF_6$ alone was catalytically inactive, giving unreacted **1a** in 95% recovery (entry 8). Compound **3a** has a *Z*-configuration according to its ^{1}H NOE spectra.[9]

We assessed the reactions using *α*-aryl vinylazides **2b-d** (2.0 equiv) bearing various substituents (X = *t*-Bu, Cl, OMe) and propargyl ester **1b** (1.0 equiv). The reactions were performed with P(*t*-Bu)$_2$(*o*-biphenyl)AuCl/$AgSbF_6$ (10 mol%) in hot DCE (80 °C) for 24 h to allow complete conversion. In entries 1-3 (Table 2), the yields of desired buta-1,3-dien-2-yl ester **3b** were 33%-63% with *p*-methoxyphenyl being the least efficient because of its high basicity.

To explore the reaction mechanism, we carried out the reactions on propargyl esters **1b-1p** bearing various substituents. Table 3 shows their reactions with model vinylazide **2a** with P(*t*-Bu)$_2$(*o*-biphenyl)AuCl/$AgSbF_6$ (10 mol %) in hot DCE (80 °C) for 12-24 h**.** ^{1}H NOE spectra were recorded to elucidate the configurations of resulting products, except compounds **3l-3m** ($R^1 = R^2$). Buta-1,3-dien-2 yl esters **3b-3i** have *Z*-configurations (R^2 = H, *Z/E* > 30:1) whereas products **3j-3k** and **3o-3p** bear *E*-configurations (*E/Z* > 30:1). Various carboxylates (X = Ph and *t*-Bu) maintained the reaction efficiency, which were known to active for 1,2-carboxylate shifts[10-11] (entries 1-2). Among propargyl esters **1d-g** bearing various 4-phenyl substituents (entries 3-6), electron-rich phenyl groups (Me or OMe) provided better product yields (82-84%) than their electron-deficient analogues **3f** and **3g** (Cl, Br; 56-66%). This trend reflects the relative ease of a 1,2-benzoyloxy shift.[10-11] The molecular structure of compound **3e** was confirmed by X-ray diffraction study.[12] Electron-rich 2-furyl and 3-thienyl-derived substrates **1g** and **1h** resulted in 60-68% yields as their small sizes were not favorable for a 1,2-benzoyloxy shift (entries 7-8). We tested the reactions on alkenyl and alkynyl substituents **1j** and **1k**, preceding to desired products **3j** and **3k** in 61% and 74% respectively, albeit in *E*-configurations (*E/Z* > 30:1, entries 9-10). 3,3-Disubstituted propargyl esters **1l-1p** were very favorable for this benzoyloxy shift,[10-11] delivering desired **3l-3p** in 72-80% yields (entries 11-15). In Table 3, the substituent effects of propargyl esters enable us to conclude that 1,2-carboxylate shifts affect the reaction efficiency whereas distinct *Z*- and *E*-regioselectivities deserve mechanistic consideration.

Eq 5 shows that the transformation of buta-1,3-dien-2-yl ester **3k** into 4-benzylidene cyclopent-3-en-1-one **5** catalyzed by P(*t*-Bu)$_2$(*o*-biphenyl)AuCl/$AgSbF_6$ (5 mol %) in DCE (60 °C, 20 h); the resulting product **5** was present as *E/Z* regioisomers (*E:Z* = 4:1) with a combined 90% yield. Compound **5** was not observed in the course of the formation of buta-1,3-dien-2-yl ester **3k** (Table 3, entry 10) because vinylazides likely reduce the acidity of gold catalysts. Vinylazides can undergo thermal rearrangement to 2*H*-azirines at elevated temperatures.[8]

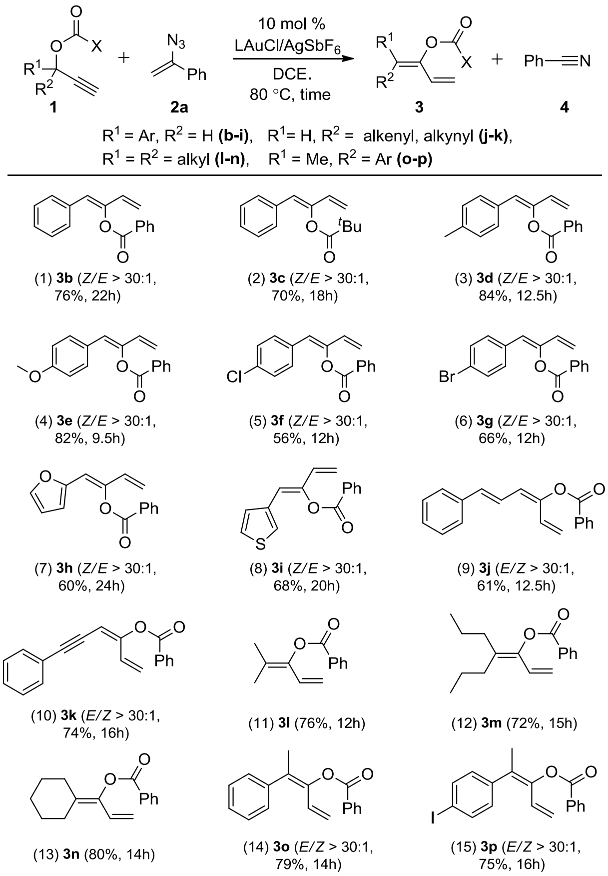
Table 2. Gold-catalyzed reaction of various vinylazides with propargyl ester



Entry	Azide **2**	*t* (°C)	*t* (h)	yield (%)^{a,b}	
				3b	**4**
1	X= *t*-Bu **(2b)**	80	24	55	**(4b)** 51
2	X= Cl **(2c)**	80	24	63	**(4c)** 58
3	X= OMe **(2d)**	80	30	33	**(4d)** 32

[a]**1b** (0.141 M, 1.0 equiv), **2** (2.0 equiv), [b]Product yields are given after purification from a silica column, L = P(*t*-Bu)$_2$(*o*-biphenyl).

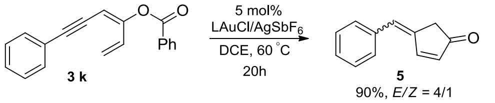
Table 3. Gold-catalyzed reaction of various propargyl esters with vinylazide



(1) **3b** (*Z/E* > 30:1, 76%, 22h)
(2) **3c** (*Z/E* > 30:1, 70%, 18h)
(3) **3d** (*Z/E* > 30:1, 84%, 12.5h)
(4) **3e** (*Z/E* > 30:1, 82%, 9.5h)
(5) **3f** (*Z/E* > 30:1, 56%, 12h)
(6) **3g** (*Z/E* > 30:1, 66%, 12h)
(7) **3h** (*Z/E* > 30:1, 60%, 24h)
(8) **3i** (*Z/E* > 30:1, 68%, 20h)
(9) **3j** (*E/Z* > 30:1, 61%, 12.5h)
(10) **3k** (*E/Z* > 30:1, 74%, 16h)
(11) **3l** (76%, 12h)
(12) **3m** (72%, 15h)
(13) **3n** (80%, 14h)
(14) **3o** (*E/Z* > 30:1, 79%, 14h)
(15) **3p** (*E/Z* > 30:1, 75%, 16h)

[a]**1** (0.141 M, 1.0 equiv), **2a** (2.0 equiv), [b]Product yields are given after purification from a silica column, L = P(*t*-Bu)$_2$(*o*-biphenyl).

2*H*-Azirine **6a** was prepared from vinylazide **2a** to examine its chemical reactivity. Under optimized condition, a mixture of propargyl ester **1b** and 2*H*-azirine **6a** with P(*t*-Bu)$_2$(*o*-biphenyl)AuCl/AgSbF$_6$ (10 mol %) in DCE (80 °C, 16 h), produced undesired dimeric product **6b**[13] with starting **1b** in 80% recovery (eq 6). This observation precludes the involvement of 2*H*-azirine **6a** in our reaction system.



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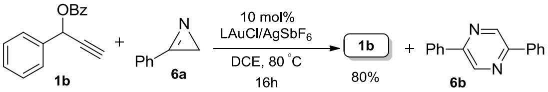
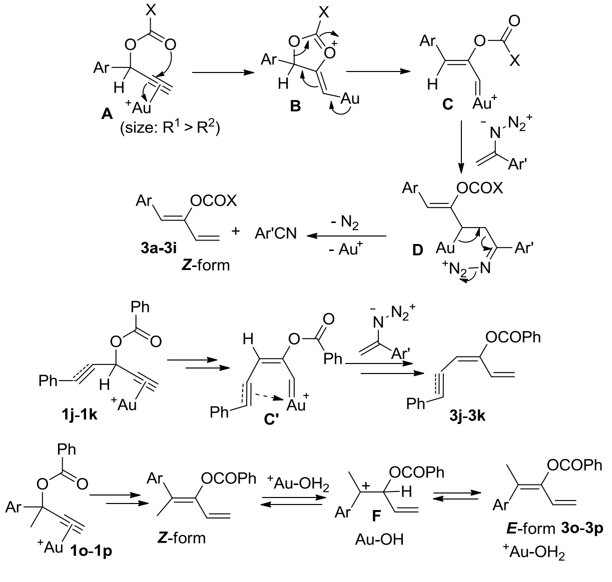


(6)

We propose a mechanism to rationalize the formation of *Z*- and *E*-configured buta-1,3-dien-2-yl esters, as depicted in Scheme 1 For most propargylic esters **1a-1i** a gold-catalyzed 1,2-carboxylate shift[10-11] is expected to form gold carbenes **C** that has preferably hydrogen cis to gold fragments to minimize steric hindrance. Although a vinylazide might attack at an electrophile at the nitrogen centers,[8] such a regioselectivity fails to rationalize the resulting buta-1,3-dien-2-yl ester. Instead, a vinyl attack of vinylazide **2a** at gold carbenes **C** is expected to form intermediate **D** that subsequently undergoes a loss of N$_2$, further inducing a cleavage of the single CH$_2$-CPh bond and the elimination of a gold fragment. This mechanism rationalizes most resulting products including **3a-3i** (R$_2$ = H) which have *Z*-configurations.

We performed DFT-calculations (B3LYP/6-31G*) of buta-1,3-dien-2-yl esters **3j-3k** and **3o-3p** to understand the relative energies of their *Z*/*E* isomers in DCE; the data were provided in Supporting Information (Table S1). For alkenyl and alkynyl-derived products **3j** and **3k**, their resulting *E*-isomeric products are less stable than their *Z*-isomers by 1.65 kcal/mol and 0.59 kcal/mol respectively; the corresponding *Z*/*E* ratios are 16.6:1 and 2.9:1 for species **3j** and **3k** respectively. This information reveals that the formation of *E*-configured **3j** and **3k** are not thermodynamically controlled, but the *E*-form of buta-1,3-dien-2-yl ester **3o** is more stable than its *Z*-isomer by 1.45 kcal/mol in DCE, corresponding to a *E*/*Z* ratio of 8.2.



Scheme 1 A plausible mechanism.

For alkynyl- and alkenyl- substituted propargyl esters **1j-1k**, we postulate that their initial gold carbenes **C'** have a π-bond motif cis to gold to attain a remote interaction, thus giving *E*-configured products **3j-3k** exclusively. For 3,3-disubstituted propargyl esters **1o-1p**, their initial *Z*-configured isomers become catalyzed with Brønsted acid LAu(OH$_2$)$^+$ in hot DCE (80 °C) to give thermodynamically favourable *E*-configured products because their corresponding intermediates **F** are stable tertiary carbocations.

In summary, gold catalyzed synthesis of buta-1,3-dien-2-yl esters from propargyl esters and vinylazides is described; the utility of these reactions is manifested by their applicability toward propargyl esters over a reasonable range. We postulate a mechanism involving an initial 1,2-carboxylate shift of propargylic esters to form gold-carbenes that are subjected to the attack of vinylazides at the C-regioselectivity. This mechanism predicts *Z*-configured buta-1,3-dien-2-yl esters to be generated under kinetic control. Under the reaction conditions, some *Z*-configured esters were catalyzed with either gold-coordination or Brønsted acid-isomerization to form *E*-isomers.

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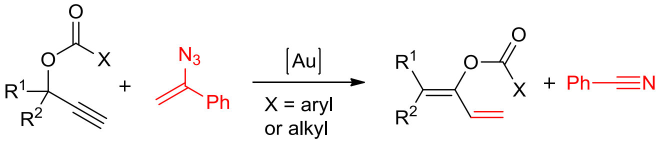

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