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Au/Ag-Catalyzed Intramolecular Ring-Opening of Vinylidene-cyclopropanes (VDCPs): An Easy Access to Functional Tetrahydropyrans

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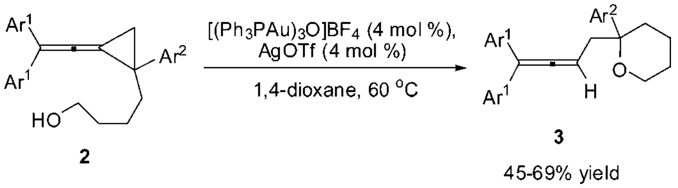
ABSTRACT



An intramolecular ring-opening of vinylidenecyclopropanes (VDCPs) tethered with alcohol chains has been established. A series of transition metal catalysts and their combinations have been screened under mild conditions, and a cocatalyst system consisting of [(Ph$_3$PAu)$_3$O]BF$_4$ (4 mol %) and AgOTf (4 mol %) was found to catalyze the reaction to completion within 10−30 min in 1,4-dioxane at 60 °C to give allene-functionalized tetrahydropyrans.

Tetrahydropyrans widely exist in naturally occurring and biologically active products, which inspired the development of creative synthetic approaches to their derivatives.[1,2] Meanwhile, relevant catalytic reactions using gold complexes have been studied actively,[3] which includes gold catalyzed-activation of alkynes,[4] allenes,[5] and alkenes.[6] However, the Au-catalyzed opening reactions of highly strained small rings have not been well documented so far.[7]

In the past several years, we and others have been engaging in chemical transformations of vinylidenecyclopropanes (VDCPs). These compounds were found to be thermally stable and adequately reactive for many important reactions in the presence of various transition metal catalysts.[8] For example, the catalytic intramolecular ring-opening/cycloaddition of VDCPs for the formation of carbocyclic or heterocyclic compounds[9] and Au-catalyzed addition of nucleophiles to unsaturated carbon−carbon bonds[4−6] have been successfully developed. During our ongoing study of VDCPs chemistry, we now design and synthesize a series of vinylidenecyclopropanes tethered with alcohol chains and explore their intramolecular ring-opening reaction. In this communication, we report the preliminary results of this

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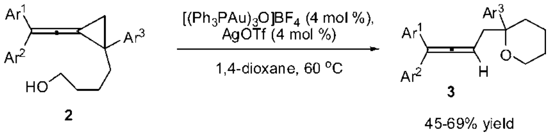
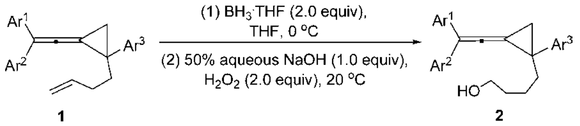
reaction for the synthesis of tetrahydropyran core structures as represented in Scheme 1.

Scheme 1. Au(I)-Catalyzed Intramolecular Addition/Ring-Opening of VDCPs **2**



Scheme 2. Synthesis of Hydroxyl Group-Attached VDCPs



*Ar^1^/Ar^2^/Ar^3^* *yield (%):*

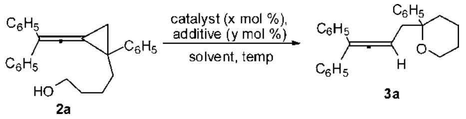
$C_6H_5/C_6H_5/C_6H_5$, **1a** (62); $C_6H_5/C_6H_5/p$-MeC_6H_4, **1b** (62);
$C_6H_5/C_6H_5/p$-$MeOC_6H_4$, **1c** (69); $C_6H_5/C_6H_5/p$-FC_6H_4, **1d** (56);
$C_6H_5/C_6H_5/p$-ClC_6H_4, **1e** (45); $C_6H_5/C_6H_5/p$-BrC_6H_4, **1f** (55);
$C_6H_5/C_6H_5/m$-BrC_6H_4, **1g** (60); p-MeC_6H_4/p-MeC_6H_4/C_6H_5, **1h** (55);
p-$MeOC_6H_4/p$-$MeOC_6H_4/C_6H_5$,1i (50); p-ClC_6H_4/p-ClC_6H_4/C_6H_5, **1j** (60);
p-$ClC_6H_4/C_6H_5/C_6H_5$, **1k**, (48).

This project started from the synthesis of the hydroxyl chain-branched vinylidenecyclopropanes (VDCPs) **2** as the substrates. Several known methods were utilized for this synthesis and were confirmed to result in either no product or in a trace ammount of product.[10] The successful procedure was realized by obtaining diarylvinylidenecyclopropanes **1** followed by the hydroboration-oxidation reaction.[11] A series of compound **2** have been successfully synthesized in moderate to good yields under mild conditions as shown in Scheme 2.

The initial experiment on the intramolecular ring-opening of VDCPs **2** was performed by subjecting them to the catalytic system consisting of AgOTf (10 mol %) as the catalyst in 1,4-dioxane at 60 °C. There is no desired product formed with nearly all starting materials **2a** unconsumed after the reaction was performed in 60 min (Table 1, entry 1). However, when $(Ph_3P)AuCl$ (5 mol %) was added into the catalytic system, the corresponding tetrahydropyran product **3a** was obtained in 41% yield along with some unknown byproduct (Table 1, entry 2). The use of $AgNTf_2$ resulted in the same yield of 41%, but $AgBF_4$ and $AgSbF_6$ only gave the yields of 24% and 19%, respectively, under above condition (Table 1, entries 3−5). Increasing the amount of $(Ph_3P)AuCl$ and AgOTf did not improve the yields (Table 1, entry 6). Pleasantly, it was found that when $[(Ph_3PAu)_3O]BF_4$ (4 mol %)[12] was used as the catalyst, **3a** can be obtained in 54% yield within a period of 90 min (Table 1, entry 7). Furthermore, when AgOTf (4.0 mol %) was used as cocatalyst together with $[(Ph_3PAu)_3O]BF_4$ (4 mol %), the reaction was greatly accelerated and can be finished within 10 min affording **3a** in 59% yield (Table 1, entry 8). Other conditions shown in Table 1 result in either complex mixture or substantially decreased chemical yields.

We next examined the scope of this reaction under the optimal condition by employing the starting materials we synthesized. As shown in Table 2, the present catalytic intramolecular ring-opening/addition proceeded smoothly to completion within 10 − 30 min for diphenylvinylidenecy-

Table 1. Condition Optimization Results



entry[a]	catalyst (x)	additive (y)	solvent	temp (°C)	time (min)	yield (%)[b] **3a**
1	–	AgOTf (10)	1,4-dioxane	60	60	0
2	$(Ph_3P)AuCl$ (5)	AgOTf (10)	1,4-dioxane	60	20	41
3	$(Ph_3P)AuCl$ (5)	$AgBF_4$ (10)	1,4-dioxane	60	40	24
4	$(Ph_3P)AuCl$ (5)	$AgNTf_2$ (10)	1,4-dioxane	60	60	41
5[c]	$(Ph_3P)AuCl$ (5)	$AgSbF_6$ (10)	1,4-dioxane	60	480	19
6	$(Ph_3P)AuCl$ (10)	AgOTf (15)	1,4-dioxane	60	60	37
7	$[(Ph_3PAu)_3O]BF_4$ (4)	–	1,4-dioxane	60	90	54
8	**$[(Ph_3PAu)_3O]BF_4$ (4)**	**AgOTf (4)**	**1,4-dioxane**	**60**	**10**	**59**
9	$[(Ph_3PAu)_3O]BF_4$ (1)	AgOTf (1)	1,4-dioxane	60	1200	38
10	$[(Ph_3PAu)_3O]BF_4$ (4)	AgOTf (4)	toluene	60	15	49
11	$[(Ph_3PAu)_3O]BF_4$ (4)	AgOTf (4)	THF	60	15	32
12	$[(Ph_3PAu)_3O]BF_4$ (4)	AgOTf (4)	THF	60	600	49
13	$[(Ph_3PAu)_3O]BF_4$ (4)	AgOTf (4)	DCE	60	5	complex
14	$[(Ph_3PAu)_3O]BF_4$ (4)	AgOTf (4)	1,4-dioxane	20	120	trace
15	$[(Ph_3PAu)_3O]BF_4$ (4)	AgOTf (4)	1,4-dioxane	80	5	complex

[a] Reaction conditions: VDCP **2a** (0.1 mmol) and $[(Ph_3PAu)_3O]BF_4$ (4 mol %) were dissolved in 1,4-dioxane (3.0 mL), and then AgOTf (4 mol %) was added. The resulted mixtures were stirred for different time at 60 °C under argon atmosphere. [b] Isolated yield. [c] Thirty-one percent of **2a** was recovered.

Scheme 3. Mechanisms of Au(I)-Catalyzed Intramolecular Addition/Ring-Opening of VDCPs

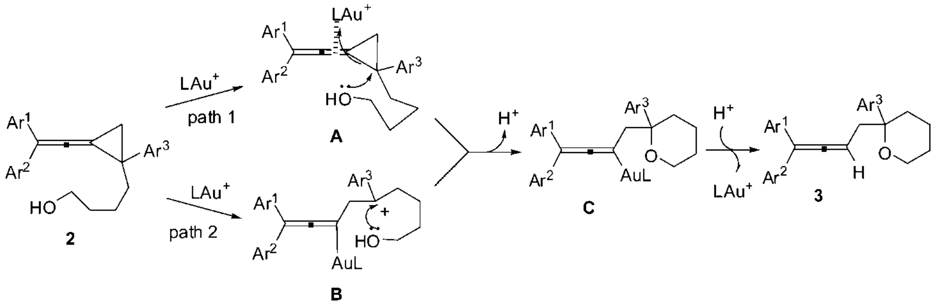
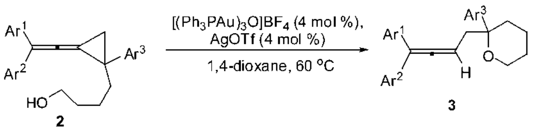


Table 2. $[(Ph_3PAu)_3O]BF_4$/AgOTf Co-Catalyzed Intramolecular Addition/Ring-Opening



entry[a]	Ar^1/Ar^2/Ar^3	time (min)	yield (%)[b] **3**
1	$C_6H_5/C_6H_5/C_6H_4$, **2b**	10	**3a**, 59
2	$C_6H_5/C_6H_5/p\text{-}CH_3C_6H_4$, **2b**	30	**3b**, 62
3	$C_6H_5/C_6H_5/p\text{-}CH_3OC_6H_4$, **2c**	30	**3c**, 69
4	$C_6H_5/C_6H_5/p\text{-}FC_6H_4$, **2d**	10	**3d**, 56
5	$C_6H_5/C_6H_5/p\text{-}ClC_6H_4$, **2e**	15	**3e**, 45
6	$C_6H_5/C_6H_5/p\text{-}BrC_6H_4$, **2f**	15	**3f**, 55
7	$C_6H_5/C_6H_5/m\text{-}BrC_6H_4$, **2g**	30	**3g**, 60
8	$p\text{-}CH_3C_6H_4/p\text{-}CH_3C_6H_4/C_6H_5$, **2h**	15	**3h**, 55
9	$p\text{-}CH_3OC_6H_4/p\text{-}CH_3OC_6H_4/C_6H_5$, **2i**	10	complex products
10	$p\text{-}ClC_6H_4/p\text{-}ClC_6H_4/C_6H_5$, **2j**	20	**3j**, 60
11	$p\text{-}ClC_6H_4/C_6H_5/C_6H_5$, **2k**	20	**3k**, 45[c]

[a] Reaction conditions: VDCP 2 (0.1 mmol) and $[(Ph_3PAu)_3O]BF_4$ (4 mol %), AgOTf (4 mol %) were dissolved in 1,4-dioxane (3.0 mL), and then the mixtures were stirred for different time at 60 °C. [b] Isolated yield. [c] **3k** was obtained as a pair of diastereoisomer (1:1). [d] It could not be cleanly isolated from some other compounds by column chromatography.

clopropanes **2b**−**2g** that bear both electron-withdrawing and electron-donating groups on their rings of Ar^3. The corresponding tetrahydropyran derivatives **3b**−**3g** were generated in moderate to good yields (Table 2, entries 1−6). Similarly, introducing moderate electron-donating or electron-withdrawing groups (Me and Cl for **2h** and **2i**, respectively) onto aromatic rings of Ar^1 and Ar^2 also afforded the corresponding tetrahydropyran derivatives **3h** and **3j** in moderate to good yields, but in the case of **2i** bearing a strong electron-donating group (MeO) on Ar^1 and Ar^2 rings, products of complex mixtures were formed (Table 2, entries 7−9). For unsymmetrical diarylvinylidenecyclopropane **2k**, the corresponding tetrahydropyran derivative **3k** was obtained as a pair of diastereoisomers with the ratio of 1:1 (Table 2, entry 10). Obviously, the present gold-catalyzed reaction should be further imporved in future so as to minimize the formation of unidentified byproducts (see the Supporting Information).

A mechanism hypothesis was proposed as shown in Scheme 3. At the beginning, Au(I) complex is oxidized to L−Au+ species by cocatalyst AgOTf prior to attacking starting material **2**. The addition/ring-opening can occur through two possible pathways: gold cation works as a Lewis acid to activate the allene functionality, affording intermediate **A** (path 1);[5] Au(I) catalyzes the ring-opening via formation of cationic intermediate **B** (path 2). The intramolecular nucleophilic addition by the hydroxyl group onto electrophilic carbon centers in intermediate **A** or **B** gives the same intermediate **C**, which produces the corresponding tetrahydropyran derivative **3** followed by protonation along with the regeneration of Au(I) catalytic species for the catalytic cycles.

In conclusion, a new intramolecular tandem addition/ring-opening of diarylvinylidenecyclopropanes (VDCPs) has been

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established for the synthesis of a variety of allene moieties containing tetrahydropyran derivatives. An efficient cocatalyst system consisting of $[(Ph_3PAu)_3O]BF_4$ (4 mol %) and AgOTf (4 mol %) was found to catalyze this reaction to completion within 10−30 min under mild conditions. The reaction showed a good scope of substrates in modest to good chemical yields and complete regioselectivity. A straightforward mechanism has been proposed for this new catalytic reaction.

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Supporting Information Available: Detailed description of experimental procedures, ^{13}C and ^{1}H NMR spectra and spectroscopic analytic data for all pure starting materials and products. This material is available free of charge via the Internet at http://pubs.acs.org.

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