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Gold(I)-Catalyzed Intramolecular Rearrangement of Vinylidenecyclopropanes

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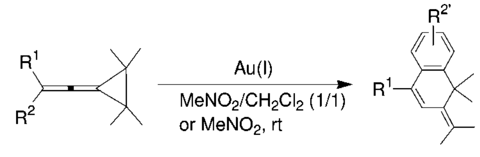

$R^1 = R^2$ = aromatic group.
or R^1 = alkyl group, R^2 = aromatic group

Vinylidenecyclopropanes **1** can undergo intramolecular rearrangement to give the corresponding functionalized 1,2-dihydronaphthalenes in the presence of gold catalyst under mild conditions. A plausible rearrangement mechanism has been proposed on the basis of control experiments.

Introduction

Skeleton rearrangements of highly strained small rings with multiple bonds and functional groups have attracted much attention from both synthetic and mechanistic viewpoints. Among these interesting substances, vinylidenecyclopropanes (VDCPs) are highly strained but readily accessible and stable molecules that serve as useful building blocks in organic synthesis.[1] Thus far, it has been known that VDCPs can undergo a variety of ring-opening/cycloaddition reactions upon heating or photoirradiation as well as in the presence of Lewis acids because the relief of ring strain can provide a powerful thermodynamic driving force.[2,3] As an interesting example, recently we have found a novel *intramolecular* rearrangement of vinylidenecyclopropane **1a** to give an unexpected naphthalene derivative **2a** via an intramolecular Friedel−Crafts reaction in the presence of hard Lewis or Brønsted acids, such as $Sn(OTf)_2$ or HOTf, along with the release of a propene molecule.[3b] We envisaged that if using gold(I), a most powerful soft Lewis acid,[4] as a catalyst, the expected *intramolecular* rearrangement product 2-isopropylidene-1,1-dimethyl-1,2-dihydronaphthalene **3a** might be obtained under mild conditions. Herein, we wish to report an interesting Au(I)-catalyzed tandem *intramolecular* rearrangement of VDCPs **1** in nitromethane or a mixed solvent of nitromethane and dichloromethane (1:1) that effectively produces 2-isopropylidene-1,1-dimethyl-1,2-dihydronaphthalene derivatives **3** in good to high yields under mild conditions, substantially enriching gold chemistry.

Results and Discussion

Initial examinations using diphenylvinylidenecyclopropane (**1a**, 0.2 mmol) having four methyl groups at the 1- and 2-position of the cyclopropane as the substrate in the presence of Ph_3PAuCl (0.01−0.02 mmol, 0.05−0.10 equiv) and AgOTf (0.01−0.02 mmol, 0.05−0.10 equiv) in dichloromethane (DCM, 2.0 mL) were aimed at determining the best conditions for this

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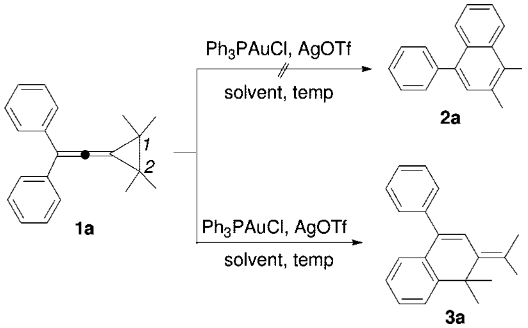
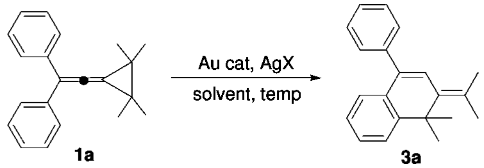
TABLE 1. Optimization of the Reaction Conditions



entry[a]	solvent	Ph_3PAuCl (mol %)	AgOTf (mol %)	temp (°C)	yield (%)[b]
1	CH_2Cl_2	10	10	−15	62
2	CH_2Cl_2	5	5	−15	64
3	CH_2Cl_2	5	5	rt	80
4	C_6H_5Me	5	5	rt	complex
5	*$MeNO_2$*	*5*	*5*	*rt*	*92*
6	MeCN	5	5	rt	no reaction
7	THF	5	5	rt	trace
8	DMSO	5	5	rt	trace
9	DMF	5	5	rt	trace
10	$ClCH_2CH_2Cl$	5	5	rt	69
11	$Cl_2CHCHCl_2$	5	5	rt	63
12	MeOH	5	5	rt	NR[c]

[a] The reactions were conducted with **1a** (0.2 mmol) in 2.0 mL of solvent. [b] Isolated yield. [c] No reaction.

TABLE 2. Optimization of the Reaction Conditions with Different Silver Salts and Phosphine Ligands



entry[a]	solvent	Au cat (mol %)	AgX (mol %)	temp (°C)	yield (%)[b]
1	$MeNO_2$	Ph_3PAuCl (10)	AgOTf (10)	rt	81
2	$MeNO_2$	Ph_3PAuCl (2)	AgOTf (2)	rt	91
3	$MeNO_2$	Ph_3PAuCl (5)	AgOAc (5)	rt	no reaction
4	$MeNO_2$	Ph_3PAuCl (5)	$AgSbF_6$ (5)	rt	87
5	$MeNO_2$	Ph_3PAuCl (5)	$AgBF_4$ (5)	rt	complex[d]
6	$MeNO_2$	Ph_3PAuCl (5)	AgOTf (5)	10	77
7	$MeNO_2$	Ph_3PAuCl (5)	AgOTf (5)	−5	87
8	$MeNO_2$	Me_3PAuCl (5)	AgOTf (5)	rt	89
9	$MeNO_2$	$(dppb)Au_2Cl_2$ (2.5)[c]	AgOTf (5)	rt	78
10	$MeNO_2$	$(2\text{-furyl})_3PAuCl$	AgOTf (5)	rt	85
11	$MeNO_2$	none	AgOTf (5)	rt	trace
12	$MeNO_2$/CH_2Cl_2 (1/1)	Ph_3PAuCl (5)	AgOTf (5)	rt	82
13	$MeNO_2$/CH_2Cl_2 (3/1)	Ph_3PAuCl (5)	AgOTf (5)	rt	79

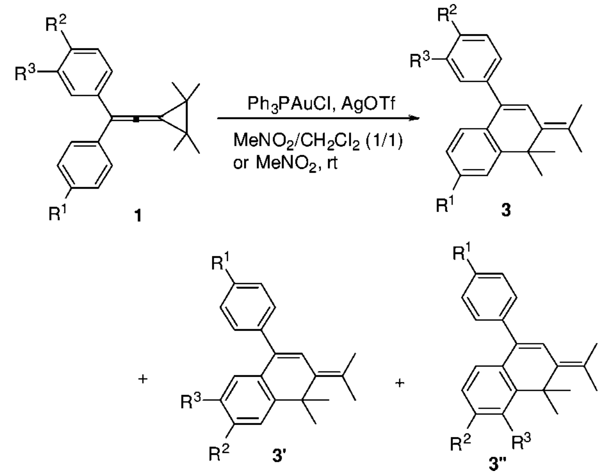
[a] **1a** (0.2 mmol) in 2.0 mL of solvent. [b] Isolated yield. [c] dppb = 1,4-bis(diphenylphosphino)butane. [d] Many unidentified products were formed.

intramolecular tandem Friedel−Crafts reaction, and the results of these experiments are summarized in Table 1. We found that, using Ph_3PAuCl (10 mol %) and AgOTf (10 mol %) as the catalysts, 2-isopropylidene-1,1-dimethyl-1,2-dihydronaphthalene **3a** was formed in 62% yield at −15 °C rather than **2a** (Table 1, entry 1). In the presence of Ph_3PAuCl (5 mol %) and AgOTf (5 mol %) at room temperature (20 °C) or at −15 °C, **3a** was obtained in 80 and 64% yields, respectively (Table 1, entries 2 and 3). In toluene, complex product mixtures were formed under identical conditions (Table 1, entry 4 as complex). In nitromethane, **3a** was obtained in 92% yield (Table 1, entry 5). Using acetonitrile (CH_3CN), tetrahydrofuran (THF), DMSO, or DMF as the solvent, either traces of **3a** were formed or no reactions occurred under the standard conditions (Table 1, entries 6−9). Using other halogenated solvents such as 1,2-dichloroethane (DCE) and 1,1,2,2-tetrachloroethane afforded **3a** in 69 and 63% yields, respectively (Table 1, entries 10 and 11). It should be noted that no reaction occurred if using methanol as a solvent, presumably due to the fact that the coordination of the oxygen atom in CH_3OH with a Au atom makes the Au complex lose catalytic ability in this reaction (Table 1, entry 12).

Next, we further optimized the reaction conditions in nitromethane with different silver salts and phosphine ligands, and the results of these experiments are summarized in Table 2. As can be seen, increasing and decreasing the employed amount of Ph_3PAuCl and AgOTf did not improve the yields of **3a** (Table 2, entries 1 and 2). Using AgOAc or $AgBF_4$ to replace AgOTf, either no reaction occurred or complex product mixtures were obtained under identical conditions (Table 2, entries 3 and 5). With $AgSbF_6$ instead of AgOTf, **3a** was obtained in 87% yield under the standard conditions (Table 2, entry 4). Changing the reaction temperature and the phosphine ligands did not significantly improve the yields of **3a** (Table 2, entries 6−10). The control experiment indicated that, without Au(I) catalyst or in the presence of AgOTf, traces of **3a** were formed (Table 2, entry 11). It should be noted that a mixed solvent of nitromethane and dichloromethane (1:1) is also suitable for this transformation (Table 2, entries 12 and 13). Therefore, the best reaction conditions are to carry out the reaction in nitromethane or a mixed solvent of nitromethane and dichloromethane (1:1) at room temperature using Au(I) (5 mol %) generated from Ph_3PAuCl (5 mol %) and AgOTf (5 mol %) as a catalyst. Although the yield of **3a** showed a little difference with 5 or 2 mol % of Au(I) catalyst, the reaction proceeded more smoothly and cleanly if using 5 mol % of Au(I) complex as the catalyst on the basis of the analysis with TLC plates.

With these optimal reaction conditions identified, we next carried out this interesting 1,2-dihydronaphthalene-forming reaction using a variety of starting materials **1**. The results of these experiments are summarized in Table 3. As can be seen from Table 3, the corresponding 1,2-dihydronaphthalene derivatives **3** were obtained in 80−99% yields in a mixed solvent of nitromethane and dichloromethane (1:1) or nitromethane (Table 3, entries 1−8 and entries 9−11). In some cases, for example, VDCPs **1b** and **1e**, 1,2-dihydronaphthalene derivatives **3** were obtained in slightly higher yields in nitromethane (Table 3, entries 1 and 9, 4 and 11). Substituents on the aromatic rings of **1** have significant influence on the yields of **3** as well as the product distribution for unsymmetrical diarylvinylidenecyclopropanes **1**. As for VDCPs **1d**, and **1f−h** bearing electron-donating groups on the aromatic ring, the corresponding 1,2-dihydronaphthalene derivatives **3** were obtained in lower yields (Table 3, entries 3, 5−7, and 10). It should be noted that, in the case of **1h**, compound **3h′** was obtained as the major product (**3h**/**3h′** = 1:6; Table 3, entry 7). In addition, using unsymmetrical diarylvinylidenecyclopropane **1e** bearing a moderately electron-withdrawing group (Cl atom) on the benzene ring as the substrate, two isomers **3e** and **3e′** were obtained in 90 and 91% yields in nitromethane or nitromethane and dichlo-

TABLE 3. **Au(I)-Catalyzed Rearrangement of 1 under These Optimized Reaction Conditions**



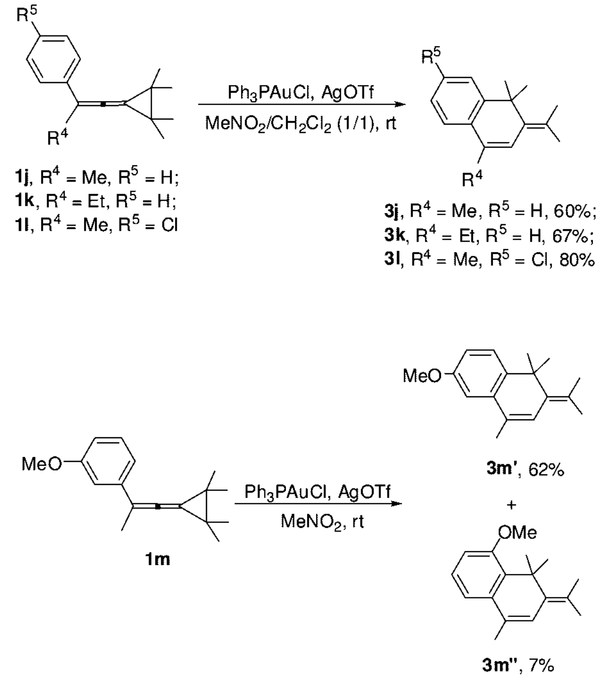
entry[a]	R^1	R^2	R^3		solvent	yield (%)[b] **3**+**3′**+**3″**
1	F	F	H	**1b**	$MeNO_2$/ CH_2Cl_2 (1/1)	**3b**, 91
2	Cl	Cl	H	**1c**		**3c**, 99
3	Me	Me	H	**1d**		**3d**, 80
4	H	Cl	H	**1e**		**3e**+**3e′**, 90 (2:1)[c]
5	H	Me	H	**1f**		**3f**+**3f′**, 80 (1:1)[c]
6	H	Me	Me	**1g**		**3g**+**3g′**+**3g″**, 85 (1.4:1.4:1)[d]
7	H	OMe	H	**1h**		**3h**+**3h′**, 86 (1:6)[c]
8	H	F	F	**1i**		**3i**+**3i′**+**3i″**, 93 (6.5:2:1)[d]
9	F	F	H	**1b**	$MeNO_2$	**3b**, 94
10	Me	Me	H	**1d**		**3d**, 86
11	H	Cl	H	**1e**		**3e**+**3e′**, 91 (2:1)[c]

[a] The reactions were conducted with **1** (0.2 mmol) in 2.0 mL of mixed solvent of nitromethane/CH_2Cl_2 (1/1) or nitromethane in the presence of Ph_3PAuCl (5 mol %) and AgOTf (5 mol %). [b] Isolated yield. [c] On the basis of ^1H NMR spectroscopic data. [d] Determined tentatively on the basis of GLC analysis.

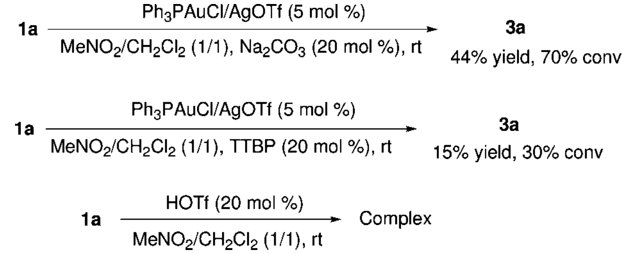
romethane (1:1) with **3e** as the major isomers, respectively, suggesting that the intramolecular Friedel–Crafts reaction preferentially takes place on the electron-rich aromatic ring (Table 3, entries 4 and 11).[5] As for unsymmetrical diarylvinylidenecyclopropane **1g** bearing two moderately electron-donating groups (methyl group) on one benzene ring as the substrate, three isomers **3g**, **3g′**, and **3g″** were obtained in 85% total yield (Table 3, entry 6). Similarly, in the case of diarylvinylidenecyclopropane **1i** having two electron-withdrawing groups (F atom) on one benzene ring as the substrate, three isomers **3i**, **3i′**, and **3i″** were obtained in 93% total yield (Table 3, entry 8).

Moreover, as for monoaromatic group substituted VDCPs **1j**, **1k**, and **1l**, the corresponding 1,2-dihydronaphthalene derivatives **3j**, **3k**, and **3l** were obtained in 60, 67, and 80% yields, indicating that the Au(I)-catalyzed rearrangement is also suitable for vinylidenecyclopropanene having one aromatic group (Scheme 1). As for VDCP **1m** having a strongly electron-donating methoxy group at the *meta*-position of the benzene ring, the corresponding products **3m′** and **3m″** were obtained in 62 and 7% yield, respectively, suggesting that the substituents on the benzene ring act in an inductive way to stabilize the intermediates (Scheme 1).

SCHEME 1. **Au(I)-Catalyzed Rearrangement of 1 under These Optimized Reaction Conditions**



SCHEME 2. **Au(I)-Catalyzed Rearrangement of 1 under These Optimized Reaction Conditions**



The control experiment shown in Scheme 2 indicated that, in the presence of Na_2CO_3 (20 mol %), **3a** was also formed in 44% yield along with 70% conversion under otherwise identical conditions. In addition, adding 20 mol % of 2,4,6-tri-*tert*-butylpyridine (TTBP) into the reaction afforded **3a** in 15% yield with 30% conversion. Moreover, using the Brønsted acid HOTf as a catalyst, complex product mixtures were obtained (Scheme 2). These results suggest that Au(I) itself catalyzes this reaction rather than the Brønsted acid HOTf.

On the basis of the above results, a plausible reaction mechanism for the formation of **3** is outlined in Scheme 3 using **1a** as a model. The corresponding cyclopropyl ring-opened zwitterionic intermediate **B** or the resonance-stabilized zwitterionic intermediate **C** is formed from the initial zwitterionic intermediate **A**. Intramolecular Friedel–Crafts reaction with the adjacent aromatic group takes place to produce zwitterionic intermediate **D**, which affords the corresponding intermediate **E** via deprotonation. Subsequent protonation of intermediate **E** produces the corresponding 1,2-dihydronaphthalene derivative **3a** along with the release of Au(I) catalyst to initiate the next catalytic cycle. When VDCPs **1** bear electron-donating groups on the aromatic ring, the key intermediate **D** is quite stable, which can provide some other byproducts through further

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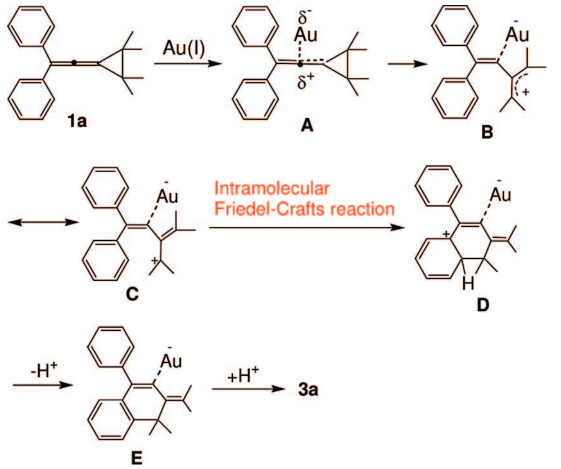
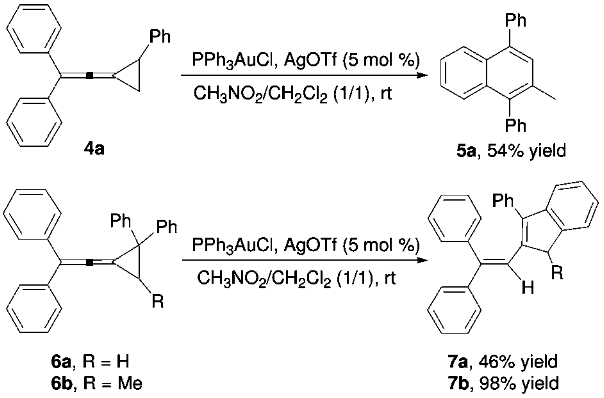
SCHEME 3. Plausible Mechanism for the Formation of 3



SCHEME 4. Au(I)-Catalyzed Rearrangement of 4a, 6a, and 6b under the Optimized Reaction Conditions



transformation, such as inter- or intramolecular Friedel−Crafts-type reaction. Therefore, the corresponding functionalized 1,2-dihydronaphthalenes **3** were formed in lower yields.

It should be noted that when using VDCPs **4a**, **6a**, and **6b** as the substrates under these optimized conditions, the corresponding naphthalene derivative **5a** and indene derivatives **7a** and **7b** were obtained in moderate to good yields, which are the same as those of the reaction products catalyzed by hard Lewis or Brønsted acid such as $Sn(OTf)_2$, $Ln(OTf)_n$ ($n = 2$ or 3), or HOTf from intermediate **C** (Scheme 4).[3a−c] This is because that, in the cases of VDCPs **4a**, **6a**, and **6b**, they are impossible to release a propene molecule as that of VDCP **1a** even in the presence of hard Lewis or Brønsted acid,[3b] and the reactions proceed through the same pathway as that catalyzed by Au(I) to provide the same reaction products.

In conclusion, we have found an interesting procedure where vinylidenecyclopropanes having four methyl groups at the 1- and 2-position of the cyclopropane undergo an interesting intramolecular rearrangement to provide functionalized 1,2-dihydronaphthalene derivatives in the presence of gold(I) catalyst through intramolecular Friedel−Crafts reaction under mild conditions. A plausible reaction mechanism has been proposed that is based on the control experiments. Further studies regarding the mechanistic details and scope of this process are in progress.

Experimental Section

General Remarks. ^{1}H NMR spectra were recorded on a 300 MHz spectrometer in $CDCl_3$ using tetramethylsilane as the internal standard. Infrared spectra were measured on a spectrometer. Mass spectra were recorded by EI method, and HRMS was measured on Kratos Analytical Concept mass spectrometer (EI or MALDI). Satisfactory CHN microanalyses were obtained with an analyzer. Melting points are uncorrected. All reactions were monitored by TLC with silica gel coated plates. Flash column chromatography was carried out using 300−400 mesh silica gel at increased pressure.

General Reaction Procedure for the Rearrangement of Diarylvinylidenecyclopropanes. To a solution of diarylvinylidenecyclopropane **1** (0.2 mmol) and Ph_3PAuCl (5 mg, 0.01 mmol) in a mixed solvent of dichloromethane and nitromethane (2.0 mL, 1:1) was added AgOTf (8 mg, 0.01 mmol), and the reaction mixture was stirred for 10 min at room temperature (monitored by TLC). After the starting materials (diarylvinylidenecyclopropanes **1**) were consumed, the solvent was removed under reduced pressure and the residue was subjected to a flash column chromatography to give the desired product **3** as a colorless liquid.

Compound 3a: A colorless liquid; IR (CH_2Cl_2) ν 3059, 2961, 2924, 2860, 1600, 1493, 1469, 1443, 1378, 1355, 779, 755, 699, 682, 594, 570, 451 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 1.06 (3H, s, CH_3), 1.30 (6H, s, $2CH_3$), 1.72 (3H, s, CH_3), 5.82 (1H, s, CH), 7.18−7.28 (3H, m, Ar), 7.34−7.44 (6H, m, Ar); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ 20.0, 24.3, 25.9, 50.4, 116.8, 119.8, 121.4, 124.7, 126.35, 126.44, 128.2, 129.0, 136.0, 136.6, 137.8, 143.0, 151.1, 153.4; MS (EI) *m*/*z* (%) 274 (M^+, 96), 259 (100), 244 (27), 229 (37), 215 (19), 202 (12); HRMS (EI) calcd for $C_{21}H_{22}O$ 274.1722, found 274.1721.

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Supporting Information Available: Spectroscopic data of all new compounds and the detailed descriptions of experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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