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Au-catalyzed isomerization of cyclopropenes: a novel approach to indene derivatives

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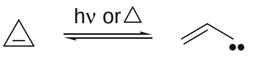
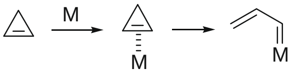
ABSTRACT

$AuPPh_3Cl/AgOTf$-catalyzed reaction of cyclopropenes is found to be highly efficient, giving indene derivatives in high yields. The reaction is suggested to proceed through gold vinyl carbenoid intermediate.

Cyclopropenes have attracted considerable attention from the synthetic community as a result of their diverse reactivities, which are attributed to their enormous ring strain.[1] The rearrangement of cyclopropene to vinyl carbene has been well investigated (Eq. 1).[2] Although the cyclopropene ring has a remarkably high strain energy, its reorganization often needs photolysis or thermolysis. Transition-metal complexes can promote or catalyze the isomerization under relatively mild conditions, although such transformations are usually substitution pattern-dependent.[3,4] In these cases, vinyl metal carbene is expected to form (Eq. 2). Pioneering investigations by Müller and Padwa have demonstrated that Rh(II) carbene species can be generated by Rh(II)-catalyzed isomerization of cyclopropenes.[4]



(1)



(2)

On the other hand, gold-catalyzed organic reactions have been extensively studied recently.[5] Gold catalysts can efficiently activate alkynes, allenes, and alkenes due to their soft Lewis acidities. Nevertheless, the activation of cyclopropenes by gold catalysts has developed much less. Very recently, Shi and co-workers reported gold-catalyzed rearrangement of vinylcyclopropenes which leads to indene derivatives.[6] Lee and co-workers reported gold-catalyzed ring-opening of cyclopropenes, leading to generation of gold vinyl carbenoid species that is trapped by alcohol.[7] These reports prompt us to disclose our own work in this field. In this Letter we report our study on Au-catalyzed reaction of cyclopropenes, which also affords indene derivatives but followed a reaction pathway different from that reported by Shi and co-workers.

At the outset of this investigation, we examined the gold-catalyzed isomerization of methyl 1,2,3-triphenylcyclopropene (**1a**). $Rh_2(pfb)_4$ [dirhodium(II) tetrakis(fluorobutyrate)]-catalyzed **1a** has been previously reported by Müller and co-workers to give indene product **2a** in high yield, but at long reaction time (48 h) at 60 °C.[4e] We found it surprising that upon catalysis with $AuPPh_3Cl/AgOTf$ in CH_2Cl_2, same product **2a** could be obtained in similarly high yield in only 30 min at room temperature (Scheme 1). This result clearly indicates that Au-catalyzed reaction of cyclopropene is much more efficient than the reaction catalyzed by the corresponding Rh(II) catalyst.

Next 1,2-diphenylcycloprop-2-enecarboxylate **3** is subjected to the same reaction conditions. Lactone **4** was isolated in 40% yield (Scheme 2). Lactone **4** should be formed by the interaction of intermediate vinyl Au carbene with the carbonyl oxygen (vide infra).

To limit the possible reaction sites for the gold carbenoid intermediate, the ester group in **3** was reduced to alcohol, which was further masked with protecting groups. Cyclopropenes **5a**–**e** were then subjected to gold catalysis (Table 1). The reactions afforded 1-methylene-2-phenyl-1*H*-indene **6a** as the major products. From

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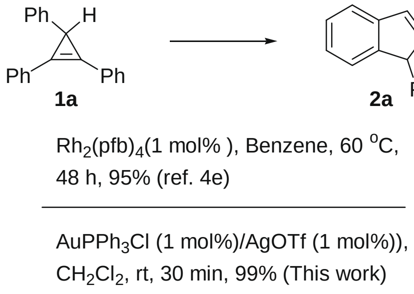
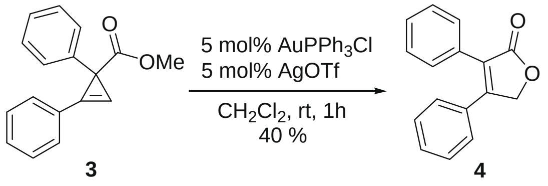


Scheme 1.



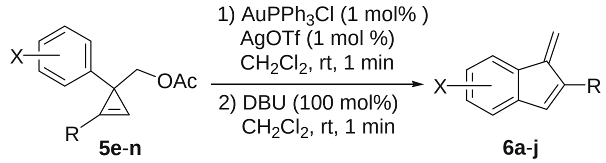
Scheme 2.

the data summarized in Table 1, it is evident that protecting group significantly affects the outcome of the reaction. The cyclopropene with acetate substituent afforded clean reaction with moderately high yield of indene product **6a** (entry 5). Further optimization of the reaction condition suggested that solvent effect was marginal (entries 5–7), with CH_2Cl_2 affording the optimal result. The reaction was found to be improved by adding DBU (entry 9).

For comparison, a series of transition-metal catalysts were examined with acetate **5e**. $Rh_2(OAc)_4$-catalyzed reaction gave only trace amount of **6a**, while the reaction with electron-deficient $Rh_2(pfb)_4$ catalyst gave mainly diene product (entry 16).[8] $PtCl_2$-catalyzed reaction afforded **6a** in low yield, while reaction with Cu(I) gave no indene product. With $AuCl_3$, the reaction gave indene in only 8% yield. It was also observed that neither $AuPPh_3Cl$ nor AgOTf alone could catalyze the reaction. Finally, as control experiment, TfOH-catalyzed reaction of **5e** was examined and it was found that no reaction occurred.

With optimized reaction conditions we proceeded to examine the scope of the isomerization with substrates **5e**–**n** (Table 2). Halide- and methyl-substitution on the phenyl at 3 position had almost no influence on the yields (entries 2–5). However, nitro substituent significantly diminished the yield (entry 6) and the expected indene product **6f** could only be isolated without the addition of DBU. On the other hand, the substituent on the C1 seemed not to affect the reaction significantly (entries 7–10).

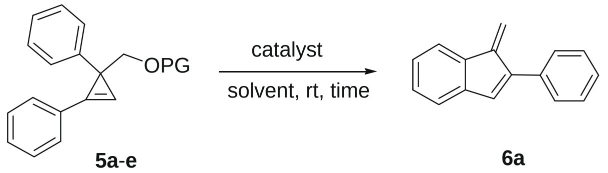
Table 2
Gold(I)-catalyzed isomerization of cyclopropene derivatives **5e**–**n**



Entry	**5**	**6**, Yield[a] (%)
1	**5e**, X = H, R = Ph	**6a**, 80
2	**5f**, X = *o*-F, R = Ph	**6b**, 82
3	**5g**, X = *p*-Me, R = Ph	**6c**, 82
4	**5h**, X = *p*-Cl, R = Ph	**6d**, 79
5	**5i**, X = *p*-Br, R = Ph	**6e**, 82
6	**5j**, X = *p*-NO_2, R = Ph	**6f**, 38[b,c]
7	**5k**, X = H, R = 1-naphthyl	**6g**, 85[c]
8	**5l**, X = H, R = 1-cyclohexenyl	**6h**, 70
9	**5m**, X = H, R = *n*-C_5H_{11}	**6i**, 90
10	**5n**, X = H, R = $PhCH_2OCH_2CH_2$	**6j**, 92[c]

[a] Isolated yield.
[b] Without adding DBU at the end.
[c] Products were easy to be polymerized.

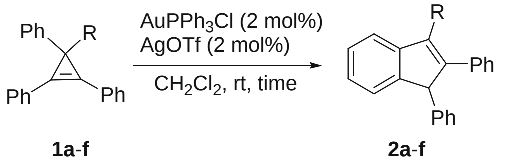
Table 1
Isomerization of Cyclopropenes under various conditions[9]



Entry	**5**, PG=	Cat (mol %)	Solvent	Time	**6a**, Yield[a] (%)
1	**5a**, H	$AuPPh_3Cl$ (5)/AgOTf (5)	CH_2Cl_2	5 min	33[b]
2	**5b**, TMS	$AuPPh_3Cl$ (5)/AgOTf (5)	CH_2Cl_2	5 min	31[b]
3	**5c**, MOM	$AuPPh_3Cl$ (5)/AgOTf (5)	CH_2Cl_2	4 h	20
4	**5d**, C(=NH)CCl	$AuPPh_3Cl$ (5)/AgOTf (5)	CH_2Cl_2	2 h	*trace*
5	**5e**, Ac	$AuPPh_3Cl$ (5)/AgOTf (5)	CH_2Cl_2	5 min	69
6	**5e**, Ac	$AuPPh_3Cl$ (5)/AgOTf (5)	CH_2NO_2	5 min	62
7	**5e**, Ac	$AuPPh_3Cl$ (5)/AgOTf (5)	$PhCH_3$	5 min	58
8	**5e**, Ac	$AuPPh_3Cl$ (1)/AgOTf (1)	CH_2Cl_2	5 min	73
9	**5e**, Ac	$AuPPh_3Cl$ (1)/AgOTf (1)	CH_2Cl_2	5 min	80[c]
10	**5e**, Ac	$AuPPh_3Cl$ (5)	CH_2Cl_2	12 h	0
11	**5e**, Ac	AgOTf (5)	CH_2Cl_2	12 h	<5
12	**5e**, Ac	$AuCl_3$ (5)	CH_2Cl_2	5 min	8
13	**5e**, Ac	$PtCl_2$(5)	CH_2C_2	2 h	11[c]
14	**5e**, Ac	CuI (5)	CH_2Cl_2	12 h	0
15	**5e**, Ac	$Rh_2(OAc)_4$ (1)	CH_2Cl_2	12 h	Trace
16	**5e**, Ac	$Rh_2(pfb)_4$ (1)	CH_2Cl_2	2 h	0[d]
17	**5e**, Ac	TfOH (5)	CH_2Cl_2	12 h	0

[a] Isolated yield.
[b] With some unkown impurity.
[c] DBU was added after the Au-catalyzed rearrangement was complete.
[d] See Ref. 8. $Rh_2(pfb)_4$: rhodium(II) heptafluorobutyrate.

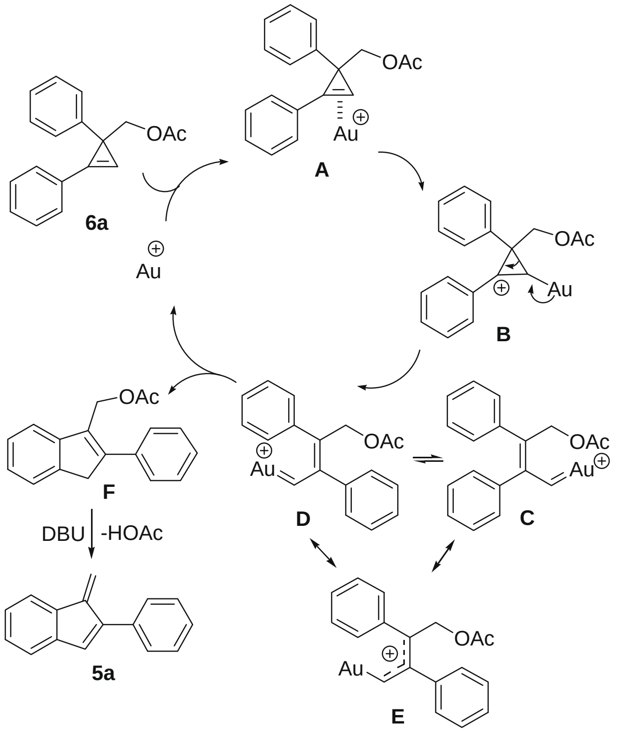
Table 3
Gold(I)-catalyzed isomerization of cyclopropene derivatives **1a**–**f**



Entry	**1**, R	Time	**2**, Yield[a] (%)
1	**1a**, H	30 min	**2a**, 99
2	**1b**, Me	15 min	**2b**, 97
3	**1c**, *n*-Bu	40 min	**2c**, 98
4	**1d**, Ph	20 min	**2d**, 97
5	**1e**, $PhC\equiv C$	6 h	**2e**, 54[b]
6	**1f**, $PhCH_2CH_2CH_2$	30 min	**2f**, 99

[a] Isolated yield.

[b] An unknown product was isolated together with **2e**.



Scheme 3.

The scope of the reaction was further demonstrated by the reaction of 1,2,3-triphenylcycloprop-1-ene derivatives **1a**–**f** under the optimized reaction conditions (Table 3). In most cases, the reaction afforded the corresponding indene derivatives in high yields. The only exception was when C3 substituent is alkynyl group, in which case the reaction took long time and the corresponding indene product **2e** was isolated in only moderate yield (entry 5).

The reaction mechanism is proposed as shown in Scheme 3. The cationic Au catalyst coordinates with the double bond of cyclopropene, leading to the formation of cyclopropyl cation regioselectively with Au at the less substituted carbon and the cation at the benzyl position. Subsequent ring-opening results in the formation of vinyl Au carbene species **C** and **D**.[10] **C** and **D** can equilibrate through the common resonance structure of Au-attached allylic cation species **E**. Direct aromatic C–H insertion by Au carbene **D** or Friedel–Crafts-type reaction of carbon cation **E** gives indene **F**, which is followed by elimination of acetic acid in the presence of base.

In summary, we have reported a highly efficient gold(I)-catalyzed isomerization of cyclopropene to indene. Gold vinyl carbenoid is suggested to be the reactive intermediate. Further exploration of these transformations is under way and will be reported in due course.

Acknowledgments

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Supplementary data

Supplementary data associated with this paper can be found, in the online version, at doi:10.1016/j.tetlet.2009.03.203.

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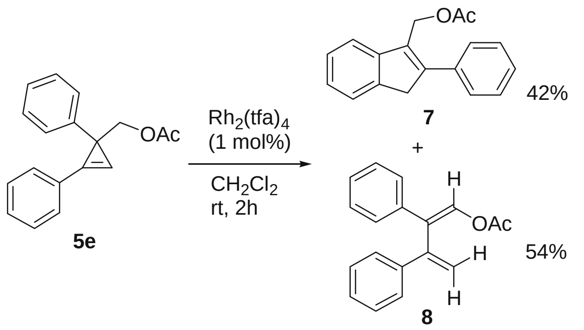

9. *Typical experiment procedures*: To CH_2Cl_2 (2 mL) were added $AuClPPh_3$ (3.3 mg, 0.0067 mmol) and AgOTf (1.7 mg, 0.0067 mmol). The resulting mixture was stirred for 5 min at room temperature. 1,2,3-Triphenyl-3-phenylpropyl cyclopropene **1f** (130 mg, 0.34 mmol), which was dissolved in CH_2Cl_2 (5 mL), was then added to the solution. The solution turned to yellow immediately. The reaction was monitored with TLC. After the substrate was consumed, the

solvent was removed in vacuo and the crude product was purified by column chromatography on silica gel with petroleum ether to give 1,2-diphenyl-3-(3-phenylpropyl)-1*H*-indene **2f** (129 mg, 99%) as yellow oil. Characterization data for **2f**: yellow oil (99% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–6.99 (m, 19H), 4.91 (s, 1H), 2.76–2.70 (m, 4H), 2.18–1.99 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.3, 145.4, 145.0, 142.0, 139.9, 139.8, 136.3, 128.8, 128.5, 128.4, 128.3, 128.1, 126.8, 126.6, 126.4, 125.8, 125.3, 123.8, 119.5, 58.1, 36.0, 30.8, 25.6; IR (neat, cm^{-1}) 3025 (w), 2933 (w), 2858 (w), 1600 (w), 1493 (m), 1452 (m); HRMS calcd for $C_{30}H_{26}$ 386.2035, found: 386.2039.

10. The gold carbenoids have been suggested as intermediates in some Au-catalyzed reactions of alkynes or allenes, see Ref. 5. Also see: Hashimi, A. S. K. *Angew. Chem., Int. Ed.* **2008**, *47*, 6754–6756.