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## Gold(I)-Catalyzed Ring Expansion of Cyclopropanols and Cyclobutanols

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Transition metal-promoted ring expansion reactions of 1-vinylcycloalkanols provide a powerful method for construction of a variety of cyclic ketones.<sup>1</sup> Similarly, 2-alkylidenecycloalkanones are potentially available from the corresponding rearrangement of 1-alkynylcycloalkanols; however, only a few examples of transition metal-catalyzed expansion of 1-alkynylcyclobutanols to alkylidenecyclopentanones have been reported.<sup>2,3</sup> A number of transformations involving the addition of heteroatom<sup>4</sup> nucleophiles or  $\pi$ -bonds<sup>5</sup> to gold(I)-activated alkynes have recently been described. We hypothesized that related cationic gold(I) complexes might be capable of catalyzing ring expansion<sup>6</sup> reactions by promoting migration of nucleophilic  $\sigma$ -bonds to alkynes.

On the basis of this hypothesis, treatment of alkynylcyclopropanol **1** with 1 mol % (PPh<sub>3</sub>)AuSbF<sub>6</sub> produced desired alkylidenecyclobutanone **2** in 95% yield as a single olefin isomer (Table 1).<sup>7</sup> The yield and rate of the rearrangement was improved by employing electron-deficient arylphosphines as ligands. For example, when the cationic gold complexes derived from tris(4-trifluoromethylphenyl)phosphinegold(I) chloride (**3**) were utilized as the catalyst, cyclobutanone **2** was produced in 99% yield after only 25 min. Conversely, the reaction was significantly less efficient when complexes bearing electron-rich ligands were employed as catalysts.

With these results in hand, we examined the scope of the tris-(4-trifluoromethylphenyl)phosphine gold(I)-catalyzed ring expansion (Table 2). A range of alkyl-substituted alkynes afforded good to excellent yields of the expected cyclobutanone products (entries 1 and 2). Aryl substituents were uniformly well tolerated with electron-withdrawing, electron-donating, and halide-substituted aryl alkynyl cyclopropanols expanding with excellent yields (entries 3–6). Notably, iodoalkynyl cyclopropanol **20** smoothly underwent expansion catalyzed by 1 mol % **3**, providing vinyl iodide **21** in 88% yield (entry 10). Trimethylsilyl and *tert*-butyldimethylsilyl ethers also undergo gold(I)-catalyzed ring expansion in excellent yields in the presence of 2 equiv of methanol (entries 7–9). The alkyne need not be substituted, as demonstrated by gold(I)-catalyzed conversion of alkyne **18** into 2-methylenecyclobutanone **19** (entry 9). Furthermore, cationic gold(I) complex **3** promotes the selective

Table 1. Ligand Effects on Au(I)-Catalyzed Ring Expansion

	HO Ph	1% LAuCl 1% AgSbF <sub>6</sub> CH <sub>2</sub> Cl <sub>2</sub> , rt		Ph
entry	ligand (L)		time	yield <sup>b</sup>
1 2 3 4	(R-	R = H R = MeO R = CI R = CF <sub>3</sub>	115 min. <sup>a</sup> 160 min. <sup>a</sup> 85 min. <sup>a</sup> 25 min. <sup>a</sup>	95% <sup>c</sup> 90% 97% 99%
5 6	<i>t</i> -Bu₃P Ph₃As		24h 24h	54% <sup>d</sup> 16%
7	Me <sup>-N</sup> ⊷ <sup>N⋅i</sup> Pr		24h	63%

 $^a$  Time to 99% conversion of 1 by <sup>1</sup>H NMR.  $^b$  Determined by <sup>1</sup>H NMR vs internal standard (mesitylene).  $^c$  5% cyclopentenone.  $^d$  13% cyclopentenone.

	R	0.5-5% [(p-C	5% Aash	P]AuCl ( <b>3</b> )			
	HO ()n	C	H <sub>2</sub> Cl <sub>2</sub> , rt	. 0	→ ~ IJ, ĸ		
entry	substrate		% cat.	time	product	yi	eld
1	HO	$R = ^{n}Hex$ (4)	1.0	12h	O R	( <b>5</b> )	81%
2	4	R = <sup>t</sup> Bu ( <b>6</b> )	0.5	6h		(7)	98%
3		X = p-Cl (8)	0.5	12h		( <b>9</b> )	94%
4		$X = \rho - CF_3$ (10)	0.5	12h	CeH4X	(11)	94%
5	06114	X = p-CN ( <b>12</b> )	0.5	12h		(13)	98%
6	7	X = p-OMe ( <b>14</b> )	0.5	12h		(15)	97%
7 <sup>b</sup>	RO,Ph	R = TMS (16)	1.0	40min.	0,Ph	( <b>2</b> )	95%
<b>8</b> <sup>b</sup>	4	R = TBS ( <b>17</b> )	1.0	4.5h		( <b>2</b> )	97%
<b>9</b> <sup>b</sup>	TBSO	(18)	1.0	50min.	° 🕂	(19)	90%°
10	HO	(20)	1.0	8h		(21)	88%
11	HO	ר (22)	1.0	12h	O Ph	( <b>23</b> )	61%
12	HO	ו (24)	5.0	48h	O Ph	(25)	74% <sup>d</sup>
13	OH	<b>≥</b> (26)	1.0	10h	$\times \not \to \circ$	(27)	73%
14	H OH	(28)	2.0	24h	H. H. H.	(29)	66%
15	OH	(30)	2.0	20h	$\sim \rightarrow \circ$	(31)	72%
16	H H	(32)	2.0	16h	440	(33)	82%

Table 2.	Scope of	Au(I)-Catalyze	d Ring Ex	pansion <sup>a</sup>
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<sup>*a*</sup> Reaction conditions: 0.5-5.0% **3** in CH<sub>2</sub>Cl<sub>2</sub>, rt. <sup>*b*</sup> MeOH (2 equiv) added. <sup>*c*</sup> Determined by <sup>1</sup>H NMR vs internal standard (mesitylene). <sup>*d*</sup> 4:1 mixture of cyclobutanone/cyclopentenone.

migration of the more substituted carbon of 2-substituted cyclopropanols **22** and **24** to afford substituted cyclobutanones **23** and **25** (entries 11 and 12).

Alkynylcyclobutanols were also found to be viable substrates for gold(I)-catalyzed ring expansion.<sup>8</sup> Reaction of cyclobutanol **26**, prepared in two steps from cyclobutanone **7**, provided 2-methylenecyclopentanone **27** in 73% yield (entry 13). Furthermore, bicyclic cyclopentanone **29** and spiro ring systems **31** and **33** were likewise obtained with selective migration of the more substituted carbon of the cyclobutanol.

We envisioned two possible mechanisms for this rearrangement (eq 1). In mechanism *a*, coordination of cationic gold(I) to the alkyne moiety induces a 1,2-alkyl shift. Mechanism *b* involves gold(I) activation of the cycloalkanol<sup>6,9</sup> to give alkyl gold(I) complex that subsequently undergoes insertion into the alkyne.<sup>10</sup> The (*E*)-



olefin geometry of the resulting alkylidene cycloalkanes<sup>11</sup> and the selective migration of more substituted cycloalkanol carbons is most consistent with mechanistic hypothesis a. Gold(I)-catalyzed rearrangement of substituted cyclopropanols 34a-d further supports mechanism a and provides insight into the stereoelectronic demands of ring expansion (eq 2). Consistent with the expected migratory aptitude, gold(I)-catalyzed rearrangement of 34a afforded only 35a. Increasing the size of the alkynyl substituent to phenyl in 34b produced a decrease in the selectivity presumably as a result of an increase in A<sup>1,3</sup> strain between the R<sup>1</sup> and R groups in proposed transition state A. This interaction is more pronounced between R<sup>2</sup> and R as demonstrated in the ring expansion of 34c, which selectively furnished cyclobutanol 36c derived from migration of the less substituted carbon.12 In accord with this hypothesis, reaction of terminal alkyne 34d favors migration of the more substituted carbon as a result of a decrease in A<sup>1,3</sup> strain between R<sup>2</sup> and R in transition state A.



Additionally, gold(I)-catalyzed ring expansion is stereospecific with respect to the migrating carbon (eq 3). *cis*-Dimethylcyclopropane **37a** quantitatively afforded *cis*-cyclobutanone **38a**, while *trans*-dimethylcyclopropane **37b** gave only *trans*-cyclobutanone **38b** in 94% yield. Benzylidenecyclobutanone **38a** was then converted into cyclobutanol **39** in two steps. Gold(I)-catalyzed ring expansion of **39** also proceeded stereoselectively to afford a 3.7:1 mixture of cyclopentanones **40** and **41** in 88% yield (eq 4).



In conclusion, we have developed a gold(I)-catalyzed ring expansion of 1-alkynylcyclobutanols and cyclopropanols to alkylidenecycloalkanones. The reaction stereoselectively provides a single olefin isomer and is stereospecific with regard to substituents on the ring. Thus, a sequence involving two gold(I)-catalyzed ring expansion reactions allows for the stereoselective preparation of a highly substituted cyclopentanone.<sup>13</sup> A mechanism involving migration of a carbon–carbon  $\sigma$ -bond onto a gold(I)-activated alkyne accounts for the observed stereoselectivity and migratory aptitude in substituted cycloalkanols. Efforts aimed at further exploiting gold(I)-catalyzed rearrangements of strained ring systems are ongoing in our laboratories.

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**Supporting Information Available:** Experimental procedures and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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