

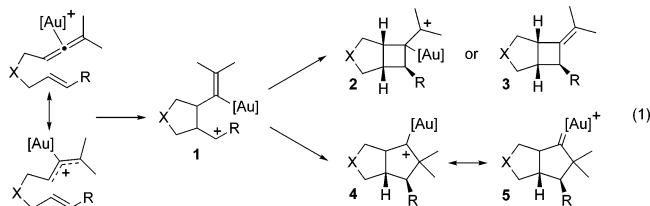
## Gold(I)-Catalyzed [2 + 2]-Cycloaddition of Allenenes

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Stabilization of cationic intermediates as gold(I)–carbenoids is proposed to be essential in a variety of gold(I)-catalyzed cycloisomerization reactions.<sup>1,2</sup> In an effort to gain further insight into the impact of this stabilization, we were inspired by parallels in the reactivity of gold-complexed allenes and allyl cations<sup>3</sup> to consider the stepwise reactions of these species with nucleophilic olefins (eq 1). Accordingly, we envisioned that addition of the alkene to a gold(I)-activated allene would generate intermediate **1**. In analogy to the formal cycloadditions of alkenes and allyl cations,<sup>4</sup> we hypothesized that the stability of the subsequent cationic species would determine which cycloadduct formed. For example, cyclobutane **3** would be produced by intramolecular trapping of cationic intermediate **1** to generate cation **2** or from its direct reaction with the carbon–gold bond.<sup>5,6</sup> Alternatively, a [3 + 2]-cycloaddition would arise via carbocation **4** which could be stabilized as carbene resonance structure **5**.<sup>7</sup>



To this end, reaction of 1,6-allenene **6** with 5 mol % of Ph<sub>3</sub>PAuCl and AgBF<sub>4</sub> in 0.1 M CH<sub>2</sub>Cl<sub>2</sub> cleanly afforded 82% yield of [2 + 2]-cycloadduct **7**<sup>8</sup> (Table 1, entry 1). Under these conditions, a variety of aryl-substituted alkenes underwent the gold(I)-catalyzed intramolecular [2 + 2]-cycloaddition with allenenes (Table 1).<sup>9</sup> For example bicyclo-[3.2.0] carbocycle **15** was formed in 80% yield from allenene **14** that does not possess a *gem*-dialkyl group in the tether (entry 5). Other C–C double bonds within the substrate do not compete with or inhibit the desired reaction (entry 2). Additional substitution at the distal position of the allene does not impact the course of the cycloaddition (entries 6 and 7). Notably, trisubstituted olefin **20** underwent gold(I)-catalyzed [2 + 2]-cycloaddition, furnishing cyclobutane **21** possessing an all-carbon quaternary center (entry 8). The diastereoselectivity relative to substituents on the tether was also examined. While substrate **22** having an allylic methyl afforded **23** in 85% yield and 6:1 dr (entry 9), allenene **24** having a methyl substituent at the allenic position afforded **25** as a single diastereomer (entry 10). Importantly, alkylidene cyclobutane **27**<sup>8</sup> was produced as a single olefin isomer from the gold-catalyzed cycloaddition of disubstituted allenene **26** (entry 11).

With these results in hand, we examined the recently developed chiral dinuclear gold(I)–biarylphosphine complexes<sup>10</sup> as catalysts for an enantioselective [2 + 2]-cycloaddition (Table 2). To this end, reaction of allenene **29** with the catalyst generated in situ from 3 mol % of (*R*)-DTBM-SEGPHOS(AuCl)<sub>2</sub> (**28**) and 6 mol % of AgBF<sub>4</sub> afforded cyclobutane **30** in 92% yield and 95% ee (Table 2, entry 1).<sup>11</sup> The gold-catalyzed reaction provided cycloadduct **17** with excellent enantioselectivity from allene **16** that is substituted at the distal carbon. Additionally, excellent enantioselectivity was

**Table 1.** Au(I)-Catalyzed [2 + 2]-Cycloaddition of Allenenes<sup>a</sup>

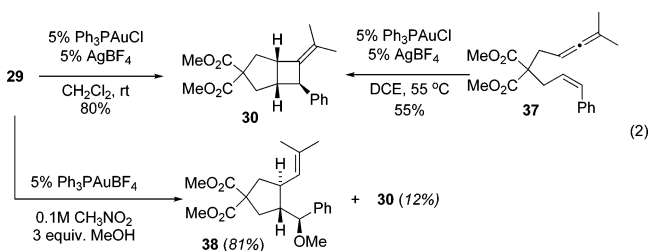
entry	substrate	time (h)	product	%yield <sup>b</sup>
1	<b>6</b> X = NTs	2	<b>7</b>	82
2	<b>8</b> X = C(CO <sub>2</sub> allyl) <sub>2</sub>	2	<b>9</b>	92
3	<b>10</b> X = C(CO <sub>2</sub> Bn) <sub>2</sub>	24	<b>11</b>	57(82) <sup>c</sup>
4	<b>12</b> X = C(SO <sub>2</sub> Ph) <sub>2</sub>	6	<b>13</b>	84
5	<b>14</b> X = CH <sub>2</sub>	7	<b>15</b>	80
6	<b>16</b> X = C(CO <sub>2</sub> Me) <sub>2</sub>	4	<b>17</b>	80
7	<b>18</b> X = C(CH <sub>2</sub> OMe) <sub>2</sub>	4	<b>19</b>	83
8	<b>20</b> E = CO <sub>2</sub> Me	2	<b>21</b>	87
9	<b>22</b> E = CO <sub>2</sub> Me	2	<b>23</b>	85 6:1 dr
10	<b>24</b> E = CO <sub>2</sub> Me	2	<b>25</b>	84 >95:5 dr
11	<b>26</b> E = CO <sub>2</sub> Me	2	<b>27</b>	80

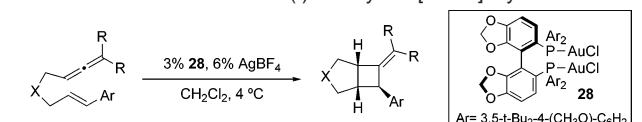
<sup>a</sup> Reaction conditions: 0.1 M allenene in CH<sub>2</sub>Cl<sub>2</sub>, 5 mol % of Ph<sub>3</sub>PAuCl, 5 mol % of AgBF<sub>4</sub>, rt. <sup>b</sup> Isolated yield after chromatography. <sup>c</sup> 0.1 M CH<sub>3</sub>NO<sub>2</sub>, 10 h, rt.

obtained in the cycloaddition of allenenes containing a variety of styrenyl aryl groups (entries 5–7).

The mechanistic hypothesis presented in eq 1 suggests that the gold(I)-catalyzed cycloaddition proceeds through a stepwise mechanism involving a series of carbocationic intermediates. In accord with a stepwise mechanism involving a benzylic cation, cyclobutane **30** was formed from the gold-catalyzed cycloaddition of *trans*- and *cis*-alkenes **29** and **37** (eq 2). Moreover, gold(I)-catalyzed reaction of **29** in the presence of methanol provided *trans*-cyclopentane **38** accompanied by a minor amount of *cis*-cyclobutane **30** (eq 3).<sup>12,13</sup>

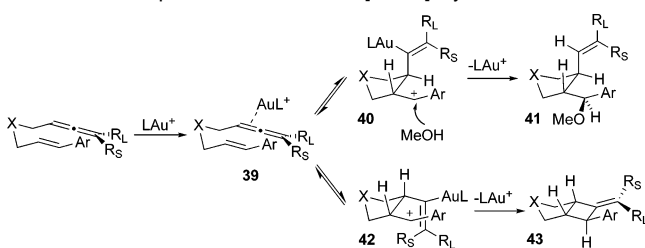
We propose the sequence outlined in Scheme 1 as the likely mechanism for the gold(I)-catalyzed reaction. Addition of the



**Table 2.** Enantioselective Au(I)-Catalyzed [2 + 2]-Cycloaddition<sup>a</sup>


entry	substrate	product	%yield <sup>b</sup>	%ee
1	<b>29</b> X = C(CO <sub>2</sub> Me) <sub>2</sub> , R = Me	<b>30</b>	92	95 <sup>c</sup>
2	<b>8</b> X = C(CO <sub>2</sub> allyl) <sub>2</sub> , R = Me	<b>9</b>	83	95
3	<b>6</b> X = NTs, R = Me	<b>7</b>	70	54 <sup>c</sup>
4	<b>16</b> X = C(CO <sub>2</sub> Me) <sub>2</sub> , R = -CH <sub>2</sub> (CH <sub>2</sub> ) <sub>3</sub> CH <sub>2</sub> -	<b>17</b>	86	95 <sup>c</sup>
5	<b>31</b> Ar = <i>p</i> -Cl-C <sub>6</sub> H <sub>4</sub>	<b>32</b>	80	96
6	<b>33</b> Ar = 2-Naphthyl	<b>34</b>	81	97
7	<b>35</b> Ar = <i>o</i> -Tolyl	<b>36</b>	78	92

<sup>a</sup> Reaction conditions: **28** (3 mol %), AgBF<sub>4</sub> (6 mol %), DCM (0.1 M), 4 °C. <sup>b</sup> Isolated yield after chromatography. <sup>c</sup> Reaction run at rt.

**Scheme 1.** Proposed Mechanism of [2 + 2]-Cycloaddition

nucleophilic alkene to gold(I)-activated allene **39** results in the formation of a carbocationic intermediate.<sup>14</sup> In the presence of methanol, kinetically formed carbocation **40** is trapped to give *trans*-cyclopentane **41**. That the cyclopentane stereochemistry of the methanol adduct is opposite to that of the cyclobutane product implies that the initial cyclization is reversible.<sup>15,16</sup> Therefore, in the absence of an exogenous nucleophile, the reaction proceeds through *cis*-disubstituted intermediate **42**. Cyclobutane **43** is then formed from reaction of the vinyl-gold with the benzylic carbocation.

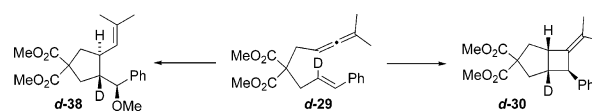
In conclusion, we have developed the first transition-metal-catalyzed cycloisomerization of allenenes to alkylidene-cyclobutanes.<sup>17,18</sup> The [2 + 2]-cycloaddition reaction provides access to enantioenriched bicyclo[3.2.0] structures using chiral biarylphosphinegold(I) complexes as catalysts.<sup>19</sup> In accord with the mechanisms of previously reported gold(I)-catalyzed cycloisomerizations, the reaction is proposed to proceed through a series of cationic intermediates. In gold-catalyzed enyne cycloisomerization reactions, the interaction of the  $\beta$ -carbon of the vinyl-gold species with a carbocation results in the formation of gold(I)-stabilized cyclopropylcarbonyl cation.<sup>2,12</sup> In contrast, the results reported herein suggest that, when this type of resonance-stabilized cation is not available, vinyl-gold species preferentially react with electrophiles to substitute the carbon-gold bond.<sup>5,20</sup> Further studies on this mechanistic dichotomy are ongoing and will be reported in due course.

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

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- (11) Under identical conditions, xylyl-BINAP(AuCl)<sub>2</sub> (85% ee) and SEGPHOS-(AuCl)<sub>2</sub> (88% ee) provided **30** with slightly lower selectivity.
- (12) For gold-catalyzed alkoxylation of enynes, see: (a) Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jiménez-Núñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. *Chem.-Eur. J.* **2006**, *12*, 1677. (b) Buzas, A. K.; Istrate, F. M.; Gagosz, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 1141. (c) Genin, E.; Leseurre, L.; Toullec, P. Y.; Genêt, J.-P.; Michelet, V. *Synlett* **2007**, *11*, 1780.
- (13) Under these conditions (CH<sub>3</sub>NO<sub>2</sub>, MeOH (3 equiv), 4 °C), reaction of **29** catalyzed by **28** afforded **38** (75%) and **30** (12%), both as racemic mixtures. See Supporting Information for additional examples of the gold-catalyzed carboalkoxylation of allenenes.
- (14) The observation that **27** was formed as a single olefin isomer suggests that this addition occurs preferentially *anti* to the phosphinegold(I) complex and *trans* to the larger allene substituent (R<sub>L</sub>) in Scheme 1).
- (15) The absence of deuterium loss in the gold(I)-catalyzed formation of *d*-**38** from *d*-**29** suggests that the methyl ether is not formed from addition of methanol to the styrene moiety of a 1,4-diene.<sup>17</sup>



- (16) Under the reaction conditions for its formation, methyl ether **38** is not formed from cyclobutane **30**.
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