DOI: 10.1002/anie.200604006

VIP Cyclopentadiene Synthesis

Gold(I)-Catalyzed Synthesis of Functionalized Cyclopentadienes[**]

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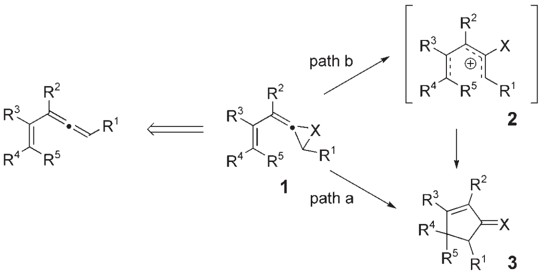
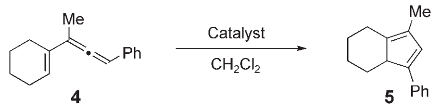
The rearrangement of vinyl allene oxides (**1**, X = O) is a key transformation in the metabolic pathway that converts arachidonic acids into cyclopentenones (**3**, X = O) [Eq (1)].[1] These rearrangements can proceed by two distinct mechanistic pathways:[2] a concerted rearrangement (path a) involving direct addition of the olefin on the epoxide or a stepwise mechanism (path b) through a Nazarov cyclization of an oxypentadienyl cation (**2**, $X = O^-$).[3] The regioselectivity of the cyclization is dictated by donation of the oxyanion into the resulting cation leading to the formation of a ketone. Recently, stabilization of developing positive charge through back-bonding from phosphinegold(I) complexes has been implicated in a number of rearrangement reactions.[4] Therefore, we hypothesized that coordination of cationic phosphinegold(I) complexes to a vinyl allene might mimic these reaction pathways through similar back-bonding, leading to metal–carbenoid intermediate **3** ($X = R_3PAu^+$).[5] These intermediates would further rearrange into substituted cyclopentadienes, important building blocks in organic and organometallic chemistry.[6,7]



(1)

In light of our recent success in using [Ph_3PAuCl] with $AgSbF_6$ in dichloromethane for carbon–carbon bond-forming reactions,[4c] we chose this system for preliminary studies of the proposed cycloisomerization (Table 1). Treatment of vinyl allene **4** with 2 mol% cationic triphenylphosphinegold(I) afforded the desired cyclopentadiene **5** as a single regioisomer in 97% yield after 1 min at 0 °C (Table 1, entry 1). Similar results were obtained when a lower temperature or lower catalyst loading were used (Table 1, entries 2 and 3). Control experiments employing either 5 mol% [Ph_3PAuCl] or 5 mol% $AgSbF_6$ as the sole catalyst did not lead to any conversion of **4** into **5** (Table 1, entries 4 and 5). Other transition-metal complexes showed no catalytic activity; however, gold(III) chloride rapidly consumed **4** to afford a small amount of **5** (Table 1, entry 6).[8]

Table 1: Catalyst optimization.



4 5

Entry	Catalyst	*T* [°C]	*t* [min]	Yield [%][a]
1	2% Ph_3PAuCl/2% $AgSbF_6$	0	1	97
2	2% Ph_3PAuCl/2% $AgSbF_6$	−20	5	93
3	1% Ph_3PAuCl/1% $AgSbF_6$	0	1	96
4	5% Ph_3PAuCl	23	180	0[b]
5	5% $AgSbF_6$	0	5	0[c]
6	5% $AuCl_3$	0	5	30[d]

[a] Yield of isolated product after column chromatography. [b] Starting material was recovered. [c] Decomposition occurred. [d] Determined by ^1H NMR spectroscopy against an internal standard (1,2,3-trimethoxybenzene).

With optimal conditions in hand, the scope of the gold(I)-catalyzed cycloisomerization of vinyl allenes was examined.[9] We were pleased to find that the reaction allowed for the regiospecific synthesis of functionalized cyclopentadienes in high yields with a variety of substitution patterns (Table 2). Substitution at the allene terminus was well tolerated, encompassing linear alkyl (Table 2, entries 8 and 9), oxygenated (entries 3–7), secondary benzyl (entry 1), and phenyl substituents (entry 2). Notably, the gold(I)-catalyzed reaction can be easily carried out on a gram scale albeit with a slightly diminished yield (Table 2, entry 1). Furthermore, the stability of acid-labile protecting groups, such as tetrahydropyranyl (Table 2, entry 9) and silyl ethers (entries 3, 4, 6, and 7), isopropylidene acetal (entry 5), and an *N*-Boc amine (entry 6), is a testament to the mildness of the reaction conditions. Bicyclic cyclopentadienes are readily produced from the cycloisomerization of vinyl allenes containing cyclic alkenes (Table 2, entries 1–6). Additionally, the gold(I)-catalyzed reaction can be employed for the synthesis of cyclopentadienes with a quaternary carbon center (Table 2, entries 2 and 3). The use of a more electron-rich gold(I) complex, [tBu_3PAuCl], as a catalyst gave improved yields for some vinyl allenes (Table 2, entries 5, 6, 8, and 9). For example, switching the gold catalyst from [Ph_3PAuCl] to [tBu_3PAuCl] resulted in an improved yield for the formation of cyclopentadiene **21** (Table 2, entry 8).

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[**] We gratefully acknowledge the University of California, Berkeley, NIHGMS (R01 GM073932-01), Merck Research Laboratories, Bristol-Myers Squibb, Amgen Inc., DuPont, GlaxoSmithKline, Eli Lilly & Co., Pfizer, AstraZeneca, and Roche for financial support.

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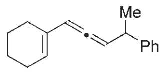
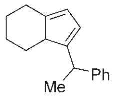
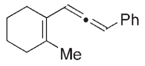
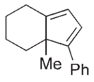
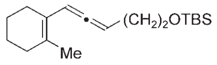
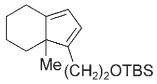
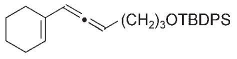
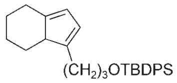
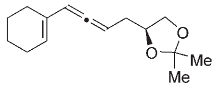
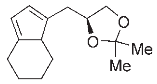
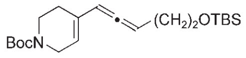
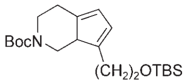
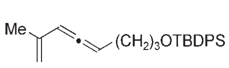
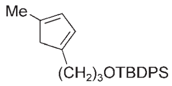
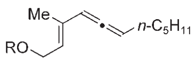
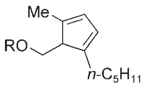
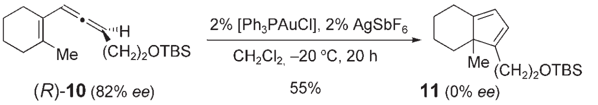
Table 2: Gold(I)-catalyzed cyclopentadiene synthesis.[a]

Entry	Vinyl allene		Cyclopentadiene		Yield [%][b]
1		**6**[c]		**7**[c]	98 (88)[d]
2		**8**		**9**	92
3		**10**		**11**	63
4		**12**		**13**	86
5		**14**[c]		**15**[c]	78[e]
6		**16**		**17**	53[e]
7		**18**		**19**	72
8		**20**: R = Bn		**21**	39 (78)[e]
9		**22**: R = THP		**23**	87[d]

[a] Reaction conditions: $[Ph_3PAuCl]$ (1.0 or 2.0 mol%), $AgSbF_6$ (1.0 or 2.0 mol%), vinyl allene in CH_2Cl_2 (0.05 M), 0°C, 5 min. [b] Yield of isolated product after column chromatography. [c] 1:1 mixture of diastereomers. [d] 5.3-mmol scale. [e] $[tBu_3PAuCl]$ (2.0 mol%) was employed. TBS = *tert*-butyldimethylsilyl, TBDPS = *tert*-butyldiphenylsilyl, Boc = *tert*-butyloxycarbonyl, Bn = benzyl, THP = tetrahydropyranyl.

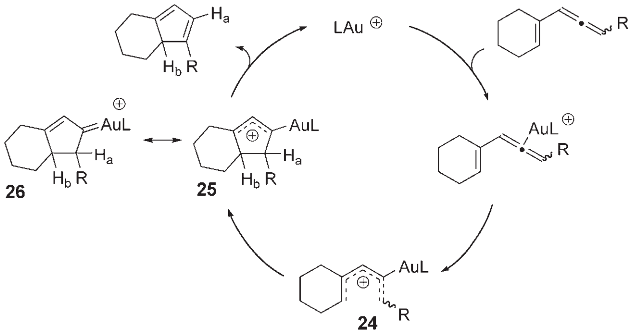
In analogy to the rearrangement of allenoxides, the two mechanistic possibilities shown in Equation (1) were considered. To distinguish between these potential mechanisms, gold(I)-catalyzed cycloisomerization of enantioenriched vinyl allene **10** was examined [Eq. (2)].[10] Treatment of vinyl allene (*S*)-**10** with 2 mol% $[Ph_3PAuCl]$ and 2 mol% $AgSbF_6$ in dichloromethane at −20°C for 20 h furnished cyclopentadiene **11** in 55% yield and with 0% enantiomeric excess. In light of recent examples of excellent chirality transfer in gold-catalyzed additions of nucleophiles to enantioenriched allenes,[11] the poor chirality transfer observed in the cyclopentadiene synthesis suggests that the reaction does not proceed through a pathway that involves direct addition of the olefin on a coordinated allene.[12]



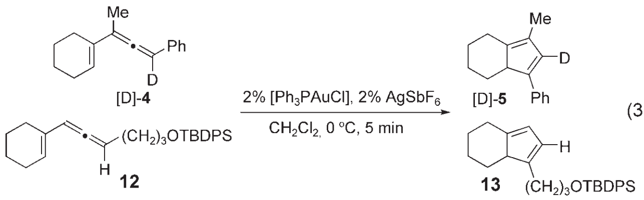
(2)

On the basis of this result, a plausible mechanism for this transformation is proposed in Scheme 1. Coordination of a cationic phosphinegold(I) to the allene results in the formation of an achiral pentadienyl cation, **24**, that undergoes electrocyclization to give the cationic intermediate **25**.[13] While regioisomeric cyclopentadienes could be formed through loss of either of two inequivalent protons (H_a or H_b) in allyl cation **25**, only a single regioisomer of the cyclopentadiene is formed. The formation of a sole cyclopentadiene product is consistent with gold(I)–carbenoid intermediate **26** undergoing an intramolecular 1,2-hydrogen shift,[4b,c] rather than a mechanism involving deprotonation/protonation of a vinyl gold intermediate. This pathway is further supported by the observation of complete deuterium incorporation into [D]-**5** and the lack of crossover in a deuterium-labeling experiment using vinyl allenes [D]-**4** and **12** [Eq. (3)].

We envisioned that the 1,2-hydrogen shift in cationic intermediate **26** could be replaced by alternative reactions. To this end, we were pleased to find that fully substituted tricyclic cyclopentadiene **28** was generated in excellent yield by reacting bicyclic vinyl allene **27** with 2 mol% cationic triphenylphosphinegold(I) at 0°C for 5 min [Eq. (4)]. Additionally, we were intrigued by the possibility



Scheme 1. Proposed mechanism for gold(I)-catalyzed cyclopentadiene synthesis.



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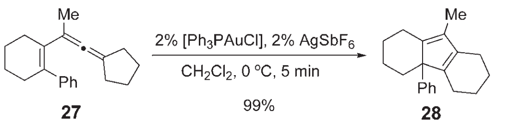
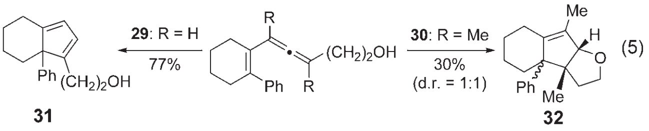


(4)

of trapping the cationic intermediate through intramolecular addition of a pendant nucleophile. To examine this possibility, vinyl allenes **29** and **30** bearing a primary alcohol were subjected to the conditions of the gold(I)-catalyzed reaction. While the gold(I)-catalyzed reaction of **29** bearing a hydrogen at the allene terminus afforded cyclopentadienyl carbinol **31** as the sole product in 77% yield, the reaction of **30** bearing a methyl group at the allene terminus led to the formation of tetrahydrofuran derivative **32** [Eq. (5)].



In conclusion, we have developed a gold(I)-catalyzed cycloisomerization of vinyl allenes for the synthesis of cyclopentadienes. The mild reaction conditions of this gold(I)-catalyzed carbon–carbon bond-forming reaction provide a regiospecific method for the synthesis of highly functionalized cyclopentadienes, including tricyclic structures through a tandem cycloisomerization/ring-enlargement reaction sequence. Application of the gold(I)-catalyzed reaction to the preparation of optically active metallocenes and asymmetric catalysis is ongoing in our laboratory and will be reported in due course.

Received: September 29, 2006

Keywords: allenes · cycloisomerization · cyclopentadienes · electrocyclic reactions · gold

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